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The Pathogenesis of Silicosis: A Review

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Introduction

The mechanism through which crystalline silica dust, alone among all inorganic dusts, produces a typical nodular hyaline lesion, has puzzled investigators for many years.

In fact, crystalline silica is unique in its ability to cause a specific disease. Whether or not silicosis can be caused only by quartz, has long been discussed, but it now appears firmly established that typical nodular silicosis can be produced only by crystalline silica. Many hypotheses have been advanced to explain the peculiar fibrogenic action of silica, but it seems that none could account for all the facts. Lately the problem has been approached from the immunological point of view.

This paper deals with some new facts, mainly immunological, in this field. It does not claim to review the whole literature on the pathogenesis of silicosis, which has been done by HOLT (1957), COLLIS (1931), and KING, MOHANTY, HARRISON and NAGELSCHMIDT (1953b).

Theories of Pathogenesis

Infective Theory

At one time the general belief was that *all mineral dusts are equally harmful for the lungs.*

According to the kind of dust, the pulmonary lesions were called anthracosis, siderosis, silicosis, etc., while differences in the biological effects of each dust went unnoticed. This is somewhat surprising because the existing differences are indeed large; some dusts are merely inert and harmless foreign bodies in the lungs, while others produce an extensive and often deadly fibrosis.

It was then believed that extensive fibrosis was either due to the combined action of dust and infection (chiefly tuberculosis), or to the peculiar hardness of some dusts.

Towards the end of the 19th and at the beginning of the 20th century, pulmonary tuberculosis was so frequent among workers employed in dusty trades, that many were led to believe that *pneumoconiosis is merely the aspect assumed by tuberculosis in a dusted lung* (see DEVOTO and CESA-BIANCHI, 1911); according to this conception the only action of the dust would be that of favouring the localization and subsequent development of tubercle bacilli in the lungs. This possibility was also supported later by some French pathologists (POLICARD, 1930, RIST and DUBROW, 1934), but in the end countless clinical and experimental data made it clear that silicosis and the other pneumoconioses are autonomous diseases, experimentally reproducible with a given dust, although tuberculous infection certainly may enhance the fibrogenic activity of the dust.

Mechanical Theory

The supporters of the autonomy of the pneumoconioses as disease entities first attributed the fibrogenic activity directly to a *mechanical action of the dusts on the lungs*. Indeed the observation that workers in softer stones appeared to suffer a less serious form of disease than workers in hard stone, and particularly in quartz, led to the conclusion that the various kinds of stone were not equally pathogenic, the harder being more pathogenic than the softer stone. It was reasonable to assume that quartz was the most pathogenic because it was the hardest. According to this line of thought the quartz particles, being very sharp and cutting, could injure and irritate the cells that had phagocytosed them, so stimulating these cells mechanically to multiplication and differentiation; this process was in accord with the then prevailing theory of irritative stimulation (VIRCHOW, 1847). Others, however, believed that the mechanically injured phagocytes eventually died and that the formation of a fibrous scar followed the destruction of the cells.

Solubility Theory

In the years from 1921 to 1924 new data emerged which lead to the rejection of the mechanical theory and gave support to the *chemical or "solubility" theory*. GYE and KETTLE (1922) pointed out the importance of the chemical factor in the behaviour of inhaled silica dust and related it to the formation of soluble silicic acid. They claimed that the supposed insolubility of silica is apparent rather than real, some degree of solution being an essential factor for the production of the cell necrosis which follows the inoculation of silica particles. Moreover, GYE and PURDY (1922, 1924) were able to produce necrosis and subsequent fibrosis of the liver and other organs by the intravenous injection of colloidal silicic acid. In those years also MAVROGORDATO (1922) was led to reject the mechanical theory and to support a chemical action of silica, after considering that "when one gets down to the order of size of 3μ and less, such terms as sharpness and hardness cease to have any appropriate meaning"; solubility and chemical inertness or activity of the dust were deemed more important. But the final blow to the mechanical theory came from GARDNER'S (1923) experiments with carborundum, which, he found, did not produce silicosis, although its particles were exceedingly hard, sharp and cutting.

Support for the chemical theory came also from some experiments by KETTLE (1926) who claimed that silica dust could produce a silicotic reaction if enclosed in a collodion bag subsequently introduced into the peritoneal cavity; in these conditions only dissolved silicic acid could conceivably pass through the pores of the collodion bag and act on the tissues. BANTING (1936), however, using Cellophane bags, could not confirm these results; although Banting's experiments should have appeared more reliable on technical grounds, they were quickly forgotten, while emphasis remained on Kettle's results. This was probably due to the fact that Banting's data, indicating that the silica particles themselves and not something dissolved from them were the noxious agents, did not match with the then prevailing opinion on the aetiology of silicosis. Recent experiments in which quartz particles enclosed in millipore membrane chambers were introduced into tissues (CURRAN and ROWSELL, 1958; PERNIS, CLERICI and GHEZZI, 1958a) have definitely confirmed Banting's conclusions.

Many other data appeared to support the solubility theory:

(a) The solubility and the fibrogenic activity of a quartz dust are both greatly depressed if the surface of the dust particles is covered with a thin layer of iron hydroxide (KETTLE, 1934) or of aluminium (DENNY, ROBSON and IRWIN, 1937).

(b) Many silicates, which are much less fibrogenic than quartz, release about only one-tenth of the soluble silica released by quartz.

(c) Sericite becomes, after treatment with HCl, both more soluble and more fibrogenic (KING, GILCHRIST and RAE, 1947).

(d) When quartz is mixed with other dusts (such as some silicates) which depress its solubility in water, it appears to become less fibrogenic (KING, *et al.*, 1947).

(e) Further support for the solution of quartz *in vivo* came from BEINTKER and MELDAU (1949), who, under the electron microscope, observed quartz particles, obtained from silicotic lungs, and noticed some appearances suggesting direct solution of silicic acid from them. It seems possible, however, that this may have taken place during the preparation for examination.

The solubility theory was convincing, yet it dealt more with the aetiology than with the pathogenesis of silicosis, inasmuch as it was centred on the definition of the noxious agent, without much attention being paid to the mechanism of the tissue reactions leading to the formation of the silicotic lesions.

Many other hypotheses were advanced to account for these tissue reactions. MAVROGORDATO (1922) believed that colloidal silicic acid did not destroy the macrophages, but on the contrary could "mummify" them, modifying their metabolism and changing them directly into fibroblasts. GARDNER (1923) thought for some time that colloidal silica, in such concentrations as can be reached *in vivo* in the clusters of phagocytes, could stimulate directly the proliferation and activity of fibroblasts. Others maintained that the necrosis of the phagocytes and of surrounding tissue cells due to silicic acid (KETTLE, 1930) or to colloidal silica hydrosol (HEFFERNAN, 1928, 1930) was the starting point of the disease, this tissue destruction being followed quite simply by scar formation. FALLON (1937), and SIMSON and STRACHAN (1940) thought that the stimulation of fibroblasts might be the consequence of the liberation from the necrotized macrophages of a phospholipid, having characteristics similar to the phosphatides of tubercle bacilli. Considering the fibrosis as a direct consequence of the action of silica, HOLT and OSBORNE (1953) believed that the macrophages, after having phagocytosed the quartz particles, might differentiate into fibroblasts. These would then secrete soluble collagen precursors that would act as a collecting site for the

silicic acid dissolved from the particles; the silicic acid adsorbed on the collagen molecules could easily polymerise (HOLT and WENT, 1960) and polymeric silica might in turn stabilize the collagen fibres by acting in a way similar to that of the acidic mucopolysaccharides of the ground substance of connective tissue.

Other workers approached the problem of the mechanism of the intracellular action of silica; KIKUTH and SCHLIPKÖTER (1956), having observed with the electron microscope alterations of the mitochondria in the cells of the developing silicotic nodule, attributed this to the action of intracellularly dissolved monomeric silicic acid, and considered different possible mechanisms by which silicic acids might interfere with the biochemical functions of the cell.

Surface Activity Theory

The study of the relationships between the solubility of silica and its fibrogenic activity, however, brought forward in the end a series of facts which were difficult to reconcile with the solubility theory. The most important of these was observed by KING, who himself had long supported the pathogenic activity of soluble silica. KING, MOHANTY, HARRISON and NAGELSCHMIDT (1953a) actually ascertained that amorphous free silica, although more soluble, was less fibrogenic than crystalline silica; and that, among the different forms of the latter, tridymite and cristobalite were less soluble but more fibrogenic than quartz. Most important was the demonstration (KING *et al.*, 1953b) that quartz becomes definitely less soluble but much more pathogenic after etching with HF or NaOH, which removes the layer of more or less disordered silica which surrounds each freshly ground quartz particle. It became obvious that some surface properties of the solid particles, possibly connected with the crystalline lattice of quartz, should play a role in the genesis of silicosis. But KING himself (1950) and others (PATERSON and WHEATLEY, 1955; SCHWARTZ and BARONETZKY, 1956) showed that under the conditions prevailing in living tissues only monomeric silicic acid could be released and that it could never reach the concentration (140 mgm./ml.) necessary for polymerization to occur. Now, while there are no doubts that polymerized, colloidal silicic acid is a powerful cytoplasmic poison (possibly as a result of its known ability to denature and precipitate proteins), there is much experimental evidence (KLOSTERKÖTTER, 1958) that monomeric silicic acid is practically innocuous. The experiments of CURRAN and ROWSELL (1958a) and of PERNIS *et al.* (1958a) already mentioned, in which quartz-containing millipore membrane capsules were implanted, are strongly against the concept of a fibrogenic activity of such silica as can dissolve *in vivo* from quartz particles. One is then forced to conclude that the pathogenic activity of quartz is a property of the particles themselves, and not of anything dissolved *in vivo* from them.

The first possible explanation for a biological activity of the quartz surface as such was proposed by the chemist JÄGER (1950, 1954) and the mineralogist SEIFERT (1950, 1954). They emphasized the peculiar pathogenic activity of *crystalline* silica and developed the somewhat over-simplified concept that the proteins adsorbed on the surface of the quartz particles might be rearranged according to the crystalline lattice of quartz itself, thus becoming fibrous. According to this theory quartz must be considered as a template on which soluble proteins are rearranged in an insoluble, fibrous, condition; any condition interfering with the adsorption of proteins on to the surface of quartz particles, such as the existence on it of a layer of aluminium, iron or even of amorphous silica, should be expected to interfere with the fibrogenic action of quartz itself. The views of Jäger and Seifert certainly had the merit of focusing attention on the surface properties of quartz particles and of providing an alternative for the theories based on the activity of soluble silica.

Other concepts have been advanced, suggesting that a catalytic activity of the surface of silica particles is the basis of their pathogenic activity. MILLER and STÖBER (1954) considered the possibility of a catalytic exchange of hydrogen atoms between proteins and the SiOH (silanol) groups existing at the surface of hydrated silica particles; THOMAS (1959) advanced his "contact theory" of silicosis based on the possibility of a surface-dependent catalytic action of silica particles on cell constituents (proteins or enzymes). An interesting extension of the views of Jäger and Seifert led SCHEEL, SMITH, VAN RIPER and FLEISHER (1954) to investigate whether serum proteins adsorbed on the surface of quartz particles might be altered so as to become auto-antigenic. They showed that the intravenous injection in rabbits of quartz particles (previously treated with homologous serum) causes the appearance in the serum of the recipient animal of a factor or factors capable of agglutinating serum-treated quartz particles; something similar to an antigen-antibody reaction was also detected by measuring the amount of nitrogen fixed by the particles after contact with "immune" rabbit serum.

Scheel's experiments were confirmed by ANTWEILER and HIRSCH (1957), by ISHINISHI and MIYAZAKI (1957) and by other Japanese investigators; SCHLIPKÖTER and DOLGNER (1958) and KLOSTERKÖTTER (1958), however, could not confirm them. While this trend of research was developing we were collecting data on the immunological reactions in the pathogenesis of silicosis, although not in the sense of a specific antibody response to proteins or any other material adsorbed and modified by quartz, but rather as a general activation of immune reactions (induced by quartz on antibody-forming tissues and cells); a detailed discussion of our results will follow later.

Considerations on the Main Trends in Research on the Pathogenesis of Silicosis in the Last Decades

Upon reconsidering the vast amount of work on the pathogenesis of silicosis summarized above, some main lines of thought are apparent. One widespread belief was that silicosis is essentially a disease with an excessive production of collagen in the lungs. This belief forced the development of research along two lines:

(1) The silicotic tissue was considered as a simple scar tissue consequent on the necrosis of macrophages and other cells due to the action of colloidal silica released from the quartz particles. With this point of view the authors probably rightly assumed that the necrosis of macrophages was the starting point of tissue reactions, leading to the formation of silicotic nodules. Strong objections, however, could be raised against the role played by soluble silica in causing the necrosis of macrophages in silicotic lesions. Moreover, considering the silicotic nodule in its spherical, expanded form as a simple scar appears incompatible with the morphology and evolution of scar tissue.

(2) Alternatively, the possibility was considered that free silica might directly induce an abnormal production of collagen fibres in the interstitial spaces. This concept has been developed in various ways:

(a) Some (MAVROGORDATO, 1922, HOLT, 1957) thought that the macrophages, after having phagocytosed silica particles, might be induced to differentiate into fibroblasts; but this possibility is not in accord with our present knowledge of macrophages; these, especially after having actually phagocytosed, must be considered as cells insusceptible of further differentiation, or transformation into another cell type.

(b) Over production of collagen fibres in the presence of silica has been proposed by HOLT either in the sense of an increased polymerization (1953) or of decreased depolymerization (1960) of soluble collagen, the action of polysilicic acid on collagen being considered to be similar to that of acidic mucopolysaccharides.

(c) Direct, acellular production of collagen fibres on simple physical grounds has been connected with the presence of crystalline silica particles in the template theory of Jäger and Seifert.

Apart from the fact that these views lack sufficient experimental support, it appears that they are centred on a single feature of the silicotic reaction, that of collagen production, neglecting other aspects. Doubtless a direct physico-chemical approach through which silica induces the production of a silicotic lesion is probably an over-simplification. The chemists, physicists and mineralogists who advanced these views received little warning from pathologists about the complexity of the cytological reactions leading to the formation of the silicotic nodule. For many decades, indeed, the prevailing description of the histogenesis of the silicotic nodule has been centred on the behaviour of macrophages and fibroblasts, the other cell types being neglected; moreover, the fact that the silicotic hyaline substance is not simple collagen arising from collagenization of the primitive reticular fibres has only recently been demonstrated.

A reconsideration of the properties and composition of the silicotic hyaline substance as well as of the cytological events which, in a complex succession, are started by the introduction of free silica particles into the living tissue, has led us to an immunological approach to the pathogenesis of silicosis.

As this approach has proved to be of heuristic value we shall deal with it in some detail, hoping that it may be useful for a better understanding of the biological problem of silicosis, and perhaps also for future research on this subject. With this in mind we shall not only give an account of the established facts, but shall also discuss some working hypotheses concerning various obscure points in the development of the events starting with the phagocytosis of the silica particles by the macrophages and ending in the formation of the typical hyaline nodules.

The Immunological Approach to the Pathogenesis of Silicosis

The Composition of the Hyaline Substance of the Silicotic Nodule

The chemical analysis of the hyaline substance (HS) isolated from human silicotic nodules (PERNIS, 1955a) showed that it is composed of proteins (80%), lipids (17%) and carbohydrates (3%). Only a part of the proteins (40%) could be accounted for by collagen, as measured by determining the hydroxyproline content of the hydrolysate of the whole tissue; the remaining 60% appeared to be due to proteins having an amino-acid composition (PERNIS and GHISLANDI, 1956) and UV absorption spectrum (PERNIS, 1955b) strikingly similar to those of serum beta or gamma globulins (fig. 1). The

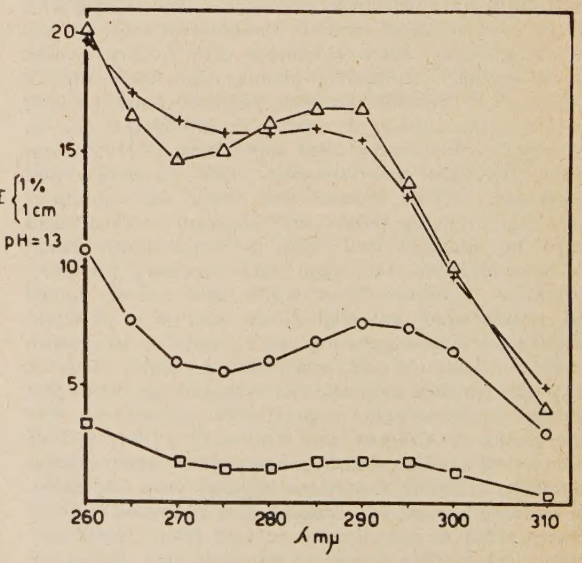

Fig. 1: U.V. Absorption spectrum of the non-collagenous proteins of human silicotic hyaline tissue, dissolved in 0,1 N NaOH.
+ Non collagenous proteins of silicotic hyaline substance.
△ Human gamma globulins.
○ Human serum albumin.
□ Collagen.

presence of considerable amounts of insoluble gamma globulins in the human HS was shown by means of the following immunological experimental results (CEPPELLINI and PERNIS, 1958):

(a) a washed homogenate of human HS injected into rabbits causes the production of anti-human-gamma-globulin antibodies;

(b) a washed homogenate of human HS absorbs selectively the anti-gamma-globulin antibodies from an anti-human equine antiserum, as can be shown by immuno-electrophoresis (fig. 2);

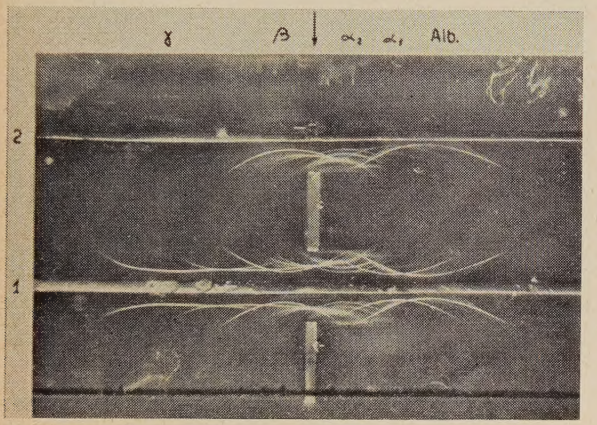

Fig. 2: Immunoelectrophoresis in agar plate.
Antigen: Normal human serum.
Antibody: (1) Equine Antiserum anti-normal-human-serum.
(2) Same antiserum absorbed with a washed homogenate of human silicotic hyaline substances.

(c) the titre of an anti-human-gamma-globulin antiserum (Coombs serum) is drastically lowered after incubation with HS, that is to say that HS gives a strongly positive anti-gamma-globulin consumption test.

The non-collagenous proteins of HS appear therefore to include a fair amount of insoluble (precipitated) gamma globulins, as detected by both chemical and immunological means. This fact, in view of the well known relationship between antibodies and gamma globulins, points to the possibility that immune reactions, involving the productions of gamma globulins, play a role in the genesis of HS; moreover, it establishes a relationship between HS and other altered connective tissues such as amyloid and some fibrinoids, which have been shown to contain gamma globulins, and which are supposed to be of immunological origin.

Spatially the amorphous precipitated globulins of HS are deposited as a mantle around collagen protofibrils, as can be seen by observation under the electron microscope of fragments of sonically disrupted HS (fig. 3); upon treatment with crystalline trypsin the globulins are dissolved, while the trypsin-resistant collagen protofibrils stand out clearly with their typical 640 Å period and appear perfectly normal (PERNIS, BAIRATI and FRIGERIO, 1956).

Fig. 3: Electron micrograph of sonically disrupted human silicotic hyaline substance: the amorphous globulin precipitate has been partially removed by the sonic treatment showing the underlying collagen fibrils.

The interfibrillar amorphous substance visible through the electron microscope certainly does not correspond to an increased and condensed connective tissue ground substance leading to the formation of a cartilage-like structure, because the chemical and chromatographic analysis of the carbohydrates of HS shows that these include only traces of acidic mucopolysaccharides (PERNIS and CLERICI, 1957) (see fig. 4).

The conclusion from these investigations was that HS is neither a degenerated collagen, nor the product of "collagenization" of reticular fibres, but the result of the precipitation of gamma globulins in the meshes of a net of normal collagen fibrils and that it corresponds to a qualitative, and not quantitative, alteration of the connective tissue. A similar phenomenon, that is the precipitation of gamma globulins on newly synthesized reticular fibrils, has been observed by WHITE, COONS and CONNOLLY (1955) in a granulomatous nodule of undisputable immunological origin, *i.e.* the nodule induced by the subcutaneous injections of antigens adsorbed on $Al_3(PO_4)_3$.

The Cytology of the developing silicotic nodule

The histological study of the developing silicotic nodule has shown that the macrophages, which have phagocytosed silica particles, undergo regressive changes and are eventually lysed, after a lag of time variable between 1–2 days and some weeks, according to the kind of dust. Tridymite and quartz etched with HF or NaOH are much more toxic for the macrophages than native quartz. Around the original cluster of macrophages,

and after these have undergone necrosis, a lively cellular reaction is observed; this consists in proliferation and collection of new macrophages, fibroblasts, mast cells in various stages of degranulation and, most interesting of all, of a considerable number of pyroninophilic cells

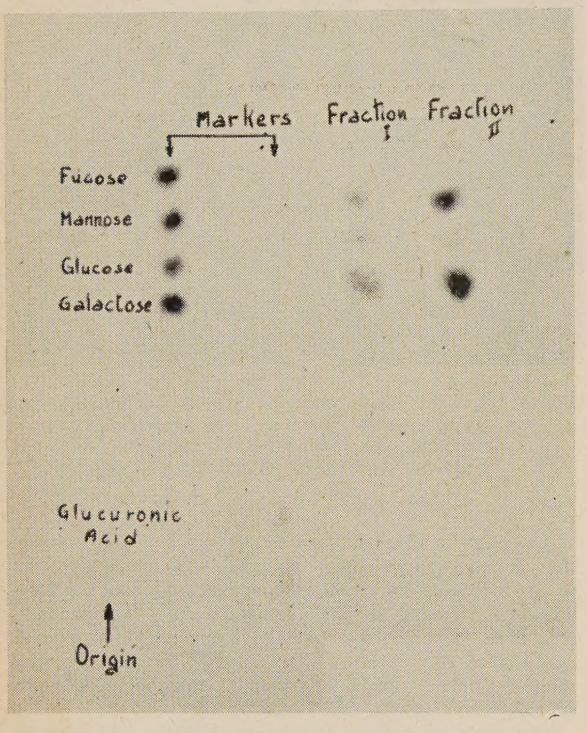

Fig. 4: Chromatographic analysis of the carbohydrates of human silicotic hyaline. Fractionation and chromatography after GLEGG *et al.* (1954): (F_I = fraction precipitated by 66% ethanol, F_{II} is precipitated by 84% ethanol). Presence of mannose, glucose, galactose and fucose, absence of hexuronic acids.

of the plasma-cell series. The latter are morphologically indistinguishable from cells which have been shown to produce antibodies (see LEDUC *et al.* 1955). BAIRATI (1960) has studied at the electron microscope ultra-thin sections of popliteal lymph nodes of rabbits that had received quartz dust, and he could observe numerous plasma cells (see fig. 5).

The fibroblasts of the silicotic nodule produce collagen fibrils, in comparatively large number, which is not unusual during the formation of granulomata including those of undisputed immunological origin (see the morphology of nodules due to adsorbed antigens); it is interesting that at the moment of maximal production of collagen, the number of degranulating mast cells also reaches its peak (PERNIS, SAFFIOTTI and TOMMASINI DEGNA, 1958b) pointing to a possible role of the acidic mucopolysaccharides of mast cells in the process of fibrillogenesis. On the other hand the cells of the plasma-cell series produce gamma globulins (for the antibody nature of these see later) that subsequently precipitate on the newly formed collagen fibres forming the core of the silicotic hyaline nodule. We have no explanation concerning the cause or causes that determine this precipitation, but again it must be pointed out that WHITE, COONS and CONNOLLY (1955) observed a similar phenomenon in their immunological granulomata. All these reactions do not easily come to an end because the silica particles set free from the necrotic macrophages are continuously taken up by new phagocytes which, in their turn, undergo regressive changes and necrosis, thus providing a continued stimulus for the cellular reactions described above.

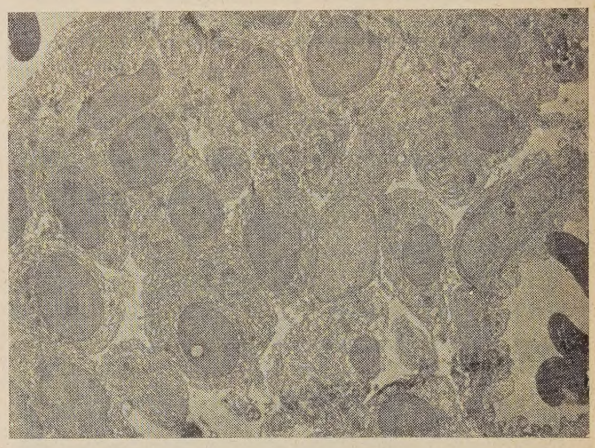

Fig. 5: Ultrathin sections of popliteal lymph node in a rabbit 45 days after injection of 50 mgr. Tridymite in the foot-pad. The node is full of plasma cells recognizable as such with the electron microscope by the well developed endoplasmic reticulum and Golgi zone.

The end result is a nodule with a hyaline core and a cellular halo composed of histiocytes, fibroblasts, mast cells, plasma cells and lymphocytes. Similar cellular reactions, with proliferation of pyroninophilic cells of the plasma-cell series, take place in the regional lymph nodes. Thus it appears that the necrosis of the quartz-laden macrophages is the starting point of the silicotic process.

Observations on the cytotoxic activity of crystalline silica particles on macrophages "in vitro"

A study of the morphology of macrophages incubated *in vitro* with crystalline silica particles (tridymite or HF-etched quartz) has shown (VIGLIANI, PERNIS and MONACO, 1960) that most cells lose their processes and swell to round balloon-like bodies; in the end they break

down, liberating cellular debris (see fig. 6 and 6 *bis*). Although this is certainly a fairly common pattern of cellular death due to loss of osmotic control by the cell membrane, it seems different in principle from the

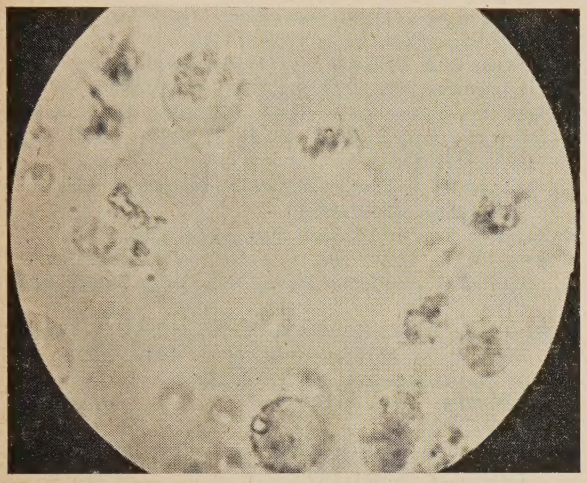

Fig. 6: Culture of rabbit macrophages from peritoneal exudate (Mackannes technic) after 24 hours of incubation with Tridymite 2,5 gm./10^6 cells. Most of the cells appear swollen and in degeneration (compare with control culture).

"mummification" of macrophages (coagulative necrosis) considered by MAVROGORDATO, but rather similar to the pattern of cellular degeneration induced in tissue cultures by activated complement (see GREENE and GOLDBERG,

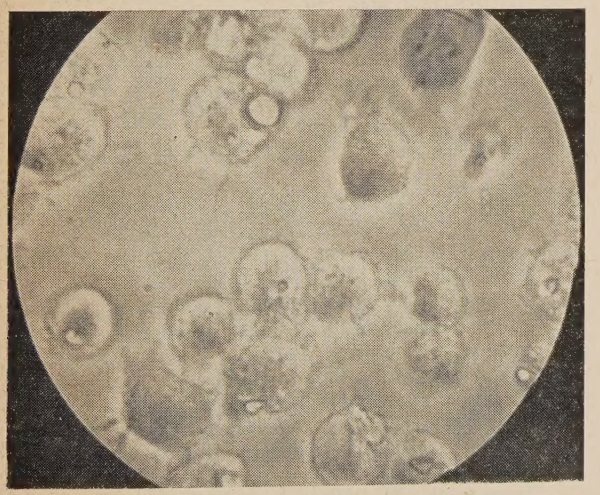

Fig. 6 bis: Control culture as 6 but without Tridymite.

1959). Moreover, the damaging effect of crystalline silica on macrophages *in vitro* can be prevented by incubating the cultures at 2°C. or by adding various complement inhibitors such as 48/80 (a histamine-liberator obtained from condensation of *p*-methoxy-phenethyl-methylamine with formaldehyde (PATON, 1951)), reduced glutathione or TAME (*p*-toluenesulphonyl-L-arginine methyl ester (TROLL, SHERRY and WACHMAN, 1954). We have therefore considered the possibility that the quartz-laden macrophages are lysed by an activated enzymatic system that has some of the properties of complement. This enzymatic system might be either complement itself or a complement-like enzyme of the macrophages, possibly an esterase (see also BAUMANN (1955) and NACHTSHEIM (1957) for interactions between quartz and an esterase/inhibitor system).

Immunological consequences of the necrosis of macrophages

The necrosis of macrophages repeatedly induced by the crystalline silica particles and the ensuing cellular reactions (particularly those of the cells of the plasma-cell series), seem to influence the immunological reactivity of the tissues where they take place. On intravenous injection of the crystalline silica particles into experimental animals, the whole reticulo-endothelial system (RES) is affected and the general immunological reactivity of the animal is modified. A series of biological effects of silica other than the fibrogenic activity become thus readily observable and measurable. These are:

(1) Increase, followed by a fall, of the phagocytic activity of the RES as measured with the carbon-clearance method of BIOZZI *et al.* (1955) (*see* PERNIS and BOLIS, 1958).

(2) Increase in resistance to Gram-negative infection (PERNIS and BOLIS, 1958).

(3) Increase of the bactericidal activity of serum (PERNIS, 1958).

(4) Increase of antibody production against an independently administered antigen such as crystalline ovalbumin (this increase may lead to an antibody response that is many times higher than that of control animals) (PERNIS, 1958).

(5) Fall in resistance to the lethal action of endotoxins (PERNIS, MAGISTRETTI and BOLIS, 1959).

(6) Appearance in the serum of non-specific immune bodies such as zymosan agglutinating factors and immunoconglutinins (PERNIS, GAMBINI and FINULLI, 1959).

These modifications of the reactivity of the RES are broadly similar to those which may be induced by treatment of experimental animals with endotoxic lipopolysaccharides, such as those of Gram-negative bacteria or those that can be extracted from mammalian cells (LANDY and SHEAR, 1957a). The effect of silica enhancing the antibody production to heteroantigens (see above, 4) may also be called an adjuvant effect, and in this respect the action of crystalline silica is

comparable in magnitude with those of other well known adjuvants such as endotoxins themselves and the components of the tubercle bacillus (Freund's adjuvant).

Analogies between the action of quartz, of endotoxins and of the tubercle bacillus

In view of the similarities indicated above between the actions of silica and those of endotoxins, and also in consideration of the necrotizing effect of silica on macrophages, it was initially thought possible (VIGLIANI and PERNIS, 1959) that substances could be set free from the macrophages which had been damaged by silica which would be similar, perhaps, to the endotoxic lipopolysaccharides extracted by LANDY and SHEAR (1957b) from mammalian cells.

An alternative hypothesis seemed worth consideration, *i.e.* that quartz particles on one side and endotoxins on the other damage the macrophages in a similar way, and that from the cells killed by either of the two, similar active substances are released; these need not necessarily be lipopolysaccharides. These latter endogenous substances would then be the actual mediators between quartz or endotoxins and the reactive RES elements. This view seems to have more points in its favour than our former one, *e.g.* the need for active complement in order that endotoxins may exert their damaging effect on cells, parallels some of the conditions that we have seen to be necessary for the necrotizing effect of silica particles on macrophages *in vitro*.

We may now return to the nature of the gamma globulins produced by the cells of the plasma-cell series in the silicotic tissues. We believe that these gamma globulins are antibodies, not only on the basis of the widespread belief that gamma globulins are always antibodies and that cells of the plasma-cell series are always antibody-producing cells (COONS, 1957–8) but also because of our experiments showing the lasting increase of antibody production in silica-treated animals (PERNIS, 1958). Accordingly the antibodies produced in the silicotic tissues would be antibodies against all the possible antigens which happen to come in contact with these tissues and which, finding a tissue in an immunologically "excited" condition, induce an abnormally large local production of the corresponding antibodies. This view is clearly at variance with that of SCHEEL *et al.* (1954), mainly because it considers quartz not as a direct or indirect antigen, but, on the contrary, as an adjuvant of antigens, similar in this respect, to endotoxins or to the Freund's adjuvant. It seems probable that there are also differences between the adjuvant effects of silica, endotoxins and Freund's adjuvant; one of these certainly may be connected with the lasting nature of the effect of quartz obviously bound to the persistence of the mineral particles in the tissue. The similarities between the adjuvant effects of quartz and the products of the tubercle bacillus open interesting possibilities for the explanation of the production of large hyaline masses (with huge amounts of precipitated gamma globulins) in the lungs of a number of patients suffering from both silicosis and tuberculosis.

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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

MATERNAL AND CHILD HEALTH

OOMEN, A. P. & SMULDERS, Frances. **Six Hundred African Prematures. A Review of the Conditions and the Results of Simple Treatment.** *Trop. & Geograph. Med.* Amsterdam. 1960, Mar., v. 12, No. 1, 15–20, 2 graphs.

This paper was written to demonstrate that much can be done to save premature babies even where accommodation and equipment are very simple. The hospital was in the Sumve area of Tanganyika and babies under 5 lb. weight were regarded as premature. Conditions favouring the premature infant were the temperature and the generous supply of mothers' milk. The regime of feeding is described, breast milk being given by tube to weakly infants until they reached 5 lb. weight.

There were 601 premature infants in the series; 101 born in the hospital had a mortality of 36% and of 500 admitted after birth 61% died. Birth weight was the main factor affecting survival. No definite cause could be given for prematurity which was common. Many mothers showed anaemia which responded rapidly to an improved diet. The data suggested that progressive deterioration of the mother's health might cause prematurity which also showed seasonal prevalence during the rains when the mothers were working intensively on the farms. A second peak of prematurity followed sale of the cash crop, the time when medical help is most often sought. Toxaemias of pregnancy and syphilis were not causative factors. Primiparae formed 35% of the mothers of premature infants, and 12% of the mothers of prematures bore twins, of whom 39% survived.

T. H. Davey

BEKEMEIER, H. Über die toxikologische Bedeutung der Salicylate. **[The Toxicological Importance of Salicylates]** *Ztschr. f. ärztl. Fortbildung.* 1960, Aug. 1, v. 54, No. 15, 859–67, 1 fig. [134 refs.]

This is a review of an extensive literature on salicylate poisoning. Salicylates are widely used as medicinal agents particularly in the United States, Canada and England. In 1949 in the United States 6,000 tons of salicylates were manufactured and it is estimated that about 4,000 tons of this total were consumed in that country in the form of acetylsalicyclic acid. There is a considerable account of the published records of salicylate poisoning. Several pages of this paper are devoted to a detailed account of the many methods of therapy which have been adopted for the treatment of such poisoning.

About 80% of all salicylate poisonings is in children who have ingested the drug accidentally in the home or have been given an over-dose in treatment. In adults poisoning results from suicidal intent or from overdosage. There are included some statistics of case mortality, an account of the diagnosis of salicylate poisoning based on 424 published cases and the results of some animal experiments on the toxicology of salicylates.

M. E. Delafield

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

SHEEN, Edith M. & DUNCAN, Ethel H. L. **A Survey of a Health Visitor's Work among the Chronic Sick and Aged in Bristol.** *Med. Officer.* 1960, Sept. 16, v. 104, No. 12, 175–80.

A special health visitor service for the aged was started in Bristol in 1950. It began with one full-time visitor: now there are 4 with supplementary help from the district health visitors.

An analysis has been made of 853 cases arising in 1950–53 and of 231 in 1957–58; the latter being only from a quarter of the City. There are now some 5,000 people on the books to whom advice and home care are given. People in need of help are brought to notice by doctors, by social workers of all types and by relatives and neighbours. The chronic sick are helped whatever their age.

A table shows that in 1950–53 10% of the total were under 60; 60% between 60 and 80 and 30% over 80. Two-thirds are women. 24% of the men and about 35% of the women were living alone and in 55% of the total there was no able-bodied person in the home; the other person, where there was one, being also decrepit. About 1 in 6 was incontinent and 1 in 17 blind or partially sighted: 1 in 10 was bed-fast at the first visit. In 80% there was no, or only 1, able-bodied person to cover the household duties, the shopping and the nursing. In the 1950–53 series 31% were adjudged to require admission to a hospital or institution but in that of 1957–58 only 21%. Among those able to stay at home 70% in the earlier group and 55% in the later had some chronic illness.

The services available, apart from the National Health Service doctor, were: home helps; a night attendant

service (12 part-time workers employed for 2 nights a week seem to be adequate for the City's population of 440,000); a daytime "sitter-in" service provided by a voluntary organization; provision of bed linen and its laundering for the incontinent, this service being partly municipal and partly voluntary; a loan service of nursing equipment such as commodes, wheel chairs, bed pulleys, T walking sticks, fireguards and bed rests; services of the Welfare Department; a "friendly visitor" service organized by voluntary bodies; "convalescence" away from home; chiropody; mobile meals, domiciliary physiotherapy; special grants from the National Assistance Board and various grants from voluntary bodies.

Special reports are sent as required to hospital authorities and to housing managers. There is a health visitors' consultative service where the present and future needs of individual cases are considered.

Reference is made to the large number of voluntary organizations available in Bristol and the point is made that they would probably develop elsewhere if the needs were publicized.

A table gives information about those admitted to institutions: 69% were "chronic, long-stay, bedridden or terminal"; 12% went into welfare institutions; 10% with acute conditions and a good prognosis went into hospital; 1% were admitted for short periods to enable the relatives to have a holiday; 6% were border-line mental cases. For many, home care had to be provided until a bed became available. A pilot scheme has been started by which transport is provided to take suitable people daily to a day hospital. An analysis has been made of the illnesses encountered in the survey. The largest percentages were: heart disease, hypertension and arterio-sclerosis 23; "frailty of old age" 20; stroke and cardio-vascular accidents 12; arthritis and rheumatism 8 and cancer 8.

The article contains particulars of a number of typical patients who have been helped.

The conclusion is "that the health visitor is a most suitable person for this type of work amongst aged and chronic sick persons". [This is a first class account of very valuable work.] *Allen Daley*

CANCER

HUEPER, W. C. & PAYNE, W. W. **Carcinogenic Studies on Petroleum Asphalt, Cooling Oil, and Coal Tar.** *Arch. Pathology.* 1960, Sept., v. 70, No. 3, 372–84, 7 figs. [Numerous refs.]

"1. Four road asphalts applied to the skin of and injected intramuscularly into mice and rats elicited cancers at the sites of application in some of these animals, attesting to the presence of carcinogenic constituents in these materials.

"2. Fumes from heated coal tar and petroleum roofing asphalt did not produce cancers of the lungs in rats and guinea pigs inhaling such fumes for a period of up to two years, although the administration of condensates of the coal tar fumes to the skin and muscle tissue of mice demonstrated the high carcinogenic potency of this matter. A roofing asphalt tested, on the other hand, proved to be noncarcinogenic to the skin of mice and rabbits.

"3. Paraffinic cooling oil fog inhaled by rats and guinea pigs elicited mainly multifocal adenomatosis in the lungs of these animals. Only one small squamous-cell carcinoma of the lung was found in a rat. A few benign and malignant tumors appeared in the skin and muscle tissue of mice following the administration of the cooling oil to these tissues, indicating a weak carcinogenic property of this paraffin oil to the tissues of mice.

"4. The various observations reported with these materials on mice and rats provide additional evidence in refutation of the allegation that sarcomas elicited in the subcutaneous tissue of rats through introduced chemicals are not genuine cancers and, therefore, do not provide proof of the carcinogenic property of the chemicals tested."

DENTAL HEALTH

RUSSELL, A. L., LITTLETON, N. W., LEATHERWOOD, E. C., SYDOW, G. E. & GREENE, J. C. **Dental Surveys in Relation to Nutrition.** *Pub. Health Rep.* Wash. 1960, Aug., v. 75, No. 8, 717–23. [22 refs.]

In the past, most dental surveys have concentrated on dental caries. Though the relation of caries to diet or nutrition has been exhaustively studied, no consistent association of dental caries with a deficiency of any known nutrient has been established.

It is postulated that periodontal disease may be more closely related to nutritional deficiency than is caries. Clinical and laboratory research has indicated that some disturbance of physiology modifies susceptibility to the disease, or its progress. This has already had some support from field studies, and this paper reports an investigation into possible relationships between periodontal status in different groups, and the physical, biochemical, or dietary findings of field teams of the U.S. Interdepartmental Committee on Nutrition for National Defense.

Investigations so far undertaken in Alaska, Ethiopia, Peru, Ecuador, and Vietnam have revealed some striking differences in the prevalence of characteristics of periodontal disease, concomitant with differences in nutrition. Details of the dental and nutritional findings in each of these countries are given. While the incidence of caries appeared unrelated to nutritional state (except for fluoridosis), and was generally low compared to that in the United States, the severity of periodontal disease was correspondingly high. Only in men in Alaska, whose thiamine and riboflavine excretion was higher (though levels of plasma-vitamin-A were lower), than in others of the same group, and in primitive Jivaro Indians in Ecuador, was periodontal disease less prevalent than in the United States; elsewhere in Alaska, and generally in Peru, incidence was comparable to that among people of low socio-economic status in the United States. In Ethiopia, Ecuador, and Vietnam prevalence was much above any recorded in the United States, and diets were unbalanced and defective.

Whether these are consistent relationships can be determined only by further analysis, and the extension of study to more populations. From these continuing analyses, more detailed reports are to be prepared.

T. P. Eddy

MENTAL HEALTH

LAMBO, T. A. **Characteristic Features of the Psychology of the Nigerian.** *West African Med. J.* 1960, June, v. 9, (n.s.) No. 3, 95–104.

This is a serious analysis of the psychology of the Nigerian and the effects of traditional methods of upbringing. The Nigerian is intensely aware of man, not only with living man but also with the dead, and this is the basis of ancestor worship. The Nigerian polygamous family is a very strong institution, in which children are important and happy; it is a warm and affectionate group, and the group is a strong unit. It is important to belong to the group.

The Nigerian tends to regard his wishes as the equivalent of actions, and to behave as if the projected wishes of others, for instance for his death, are as powerful as an act of murder; he must therefore take precautions to prevent such a wish from taking place. Hence the faith in charms and incantations, which is deeply rooted, and powerful even in some Nigerians from Westernized homes.

[It is not possible to give a satisfactory account of this thoughtful paper. It should be read in full and linked with the other contributions the author has made to an important study.] *Charles Wilcocks*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

ROSS INSTITUTE INDUSTRIAL ADVISORY COMMITTEE. LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE. **Information and Advisory Service.** Bull. No. 8, re-written June, 1960 (originally issued December, 1952), 42 pp., 28 figs. **Rural Sanitation in the Tropics.**

This pamphlet replaces one published in 1952 under the title *Sanitation for Estate and Mine Labour Forces* [this *Bulletin*, 1953, v. 28, 444]. It starts with excellent advice about latrine supervision and about educating communities provided with these facilities so that their proper use becomes a way of life. The recommendation is made that private rather than public latrines should be provided. The text has been completely rewritten and the matter is now presented in three sections dealing with family privies, public latrines and effluent disposal. The types of privy recommended for family use in villages, estates or mine compounds are, in order of preference, water-borne (cistern-flushed), water-borne (pour-flushed), the aqua privy and pit privy.

The types of public latrine recommended are the cistern-flushed water-borne and the aqua privy. The omission of the trough latrine is welcomed; in its place is proposed a double row of compartments, each pair flushing through water-seal traps into a central channel with removable cover. The methods of effluent disposal dealt with are seepage pits, soakage trenches and aeration beds.

The new edition of this valuable pamphlet is very welcome. Layout plans and pictures, and scale diagrams with measurements illustrate each form of privy

described. The diagrams are easily comprehended and the text is lucid. The installations described are suitable for most situations and for all kinds of small communities in rural areas of the tropics. The information provided will be useful to laymen as well as health staff concerned with problems of excreta disposal in the rural tropics. *T. H. Davey*

ISAAC, P. C. G. & JENKINS, D. **A Laboratory Investigation of the Breakdown of some of the Newer Synthetic Detergents in Sewage Treatment.** *J. & Proc. Inst. Sewage Purification.* 1960, Pt. 3, 314–27, 13 figs. [21 refs.] Discussion 327–9.

This paper was presented at a meeting of the Scottish Branch of the Institute of Sewage Purification held in Glasgow in October 1959. The first part of the paper is concerned with a classification of synthetic detergents, the quantities being used in the United Kingdom, the effects of detergents on sewage treatment and the receiving waters, and the chemical structure of detergents in relation to biochemical lability. In the second part of the paper there are recorded the published results of chemical experiments carried out on a considerable number of active detergent agents tested on laboratory filters and in the Warburg respirometer. Following this is an account of experiments of a current series which have been designed to study the effect of various detergents on the uptake of dissolved oxygen by sewage micro-organisms under the conditions of the BOD test. This study was made on the effect of sugar-based detergents and a new alkyl benzene sulphonate, Sodium Dobane JN, on dissolved oxygen uptake. The results of these experiments are described in detail with figures and tables. In the conclusions it is stated that a great variation in the rate of dissolved oxygen uptake in the presence of different sugar-based detergents was observed. The physical characters and chemical nature of these detergents with their trade names and the suppliers of these materials are stated.

M. E. Delafield

HOUSING

WILNER, D. M., WALKLEY, Rosabelle P., WILLIAMS, H. & TAYBACK, M. **The Baltimore Study on the Effects of Housing on Health.** *Baltimore Health News.* 1960, June, v. 37, No. 6, 45–50.

This study is a combined attempt by the Baltimore Housing Authority and City Health Department and the Johns Hopkins School of Hygiene and Public Health to unravel the effects on health of rehousing slum dwellers. Previous studies have failed to isolate rehousing from the other factors involved such as poverty, often caused by chronic illness. The references include M'GONIGLE and KIRBY'S book of 1936 (*Poverty and Public Health,* London: Victor Gollancz) where they demonstrated that in their town rehousing and the accompanying higher rents did not leave enough for adequate nutrition.

The "test" population in the Baltimore study consisted of 300 families (1,350 persons) of Negroes with low incomes rehoused in 1955 in a public housing development scheme. The "controls" were 300 other families who had applied, and were eligible, for rehousing but remained in their slum houses throughout the 3 years of the study.

By the usual survey techniques morbidity statistics were collected periodically from both groups.

This article deals mainly with persons under 20 years of age but a full comprehensive report is promised.

Tables give for each sex the episodes of illness, disabling and non-disabling, at the start of the study and during both the second and third years after the 300 families had been rehoused, with an age breakdown into 0–5, 5–9, and 10–19 years, and a further analysis of the number of days of disability divided into days in hospital, days in bed and days when kept from usual activities.

The broad result is that "the extent of illness among boys in the rehoused families was, on the average, 15% lower than that experienced by boys remaining in slum housing." Among girls it was 8% lower. An interesting feature is that the reduced morbidity is consistent at all age-groups below 20 for the second and third year after rehousing, but during the settling-in process of the first year the rehoused had more illness than the controls except for boys aged 10–19. The reason given is that in their new environment the rehoused families were a new group and met among their neighbours communicable diseases to which they had not been exposed until then. This is confirmed by the nature of the illnesses. Those with excess incidence had communicability as a principal feature, namely infective and parasitic, respiratory and digestive. This is akin to what happens when children start school or army recruits first live together in barracks. After a few months the effect of these new contacts disappears and the value of more living-space and better facilities for cleanliness is shown.

A striking finding is that accidents were one-third lower among the rehoused families: only 1% of the children played in unsafe places compared with 53% among the controls.

Preliminary findings for the adults are also given. In general, the morbidity findings are less consistent than those in the under 20 age-groups but they are definitely lower for women aged 20–34: also, their children are heavier at birth and there are fewer premature births.

[What makes this study so valuable is that it does not compare the health of the same group before and after rehousing but the rehoused are compared with a group, similar except for the rehousing, over the same period of time.] *Allen Daley*

ATMOSPHERIC POLLUTION

AMERICAN INDUST. HYG. ASS. **Air Pollution Manual. Part I. Evaluation.** pp. xx + 194, 82 figs. [Numerous refs.] 1960. Detroit 27: 14125 Prevost, Michigan, U.S.A.

This manual, prepared by a group of scientists and technologists, summarizes the information needed for the intelligent appraisal of air pollution problems and describes how this information can be obtained. As long as it is concerned with the technical problems it achieves its purpose admirably, but the discussion of non-technical, and in particular of economic, factors is largely superficial or diffuse. The emphasis is practical, and the book is divided into self-contained sections dealing with different aspects of the subject which make it an extremely useful reference book. Despite a few references to outside sources it refers to conditions in the U.S.A. and is based on experience in that country.

In the first chapter it is pointed out that pollution can be treated as a nuisance under common law, but that effective action usually requires specific legislation. In the U.S.A. interest and concern were aroused by the Donora incident in 1948, and legislation followed. The legal situations in each of the States and Territories of the Union, and in the District of Columbia, are outlined.

Chapter 2, on Community Relations, stresses the value of goodwill on both sides, and the importance of foresight in anticipating difficulties, and Chapter 3 discusses the U.S. National Air Sampling Network and outlines some of the results obtained from it (U.S. Public Health Service Publication No. 637, *Air Pollution Measurements of the National Air Sampling Network*, Washington, 1958). Chapter 4 deals with health problems but is unsatisfying largely because apart from epidemiological data little information is available.

Chapters 5 and 6, on effects on vegetation and on farm animals respectively, are of special interest, since in the U.K. at least the biological aspects have been less studied than the physical and chemical. The listing of the relative sensitivities of various plants, both wild and cultivated, to sulphur dioxide, hydrogen fluoride and "smog gases" is a particularly interesting approach.

Chapter 7, on economic aspects, is of little value, but chapters 8, 9 and 10, on Community Air Sampling, Stack Sampling and Chemical Procedure respectively, contain an enormous amount of information on these subjects, and leave no obvious gaps. The chapter on odours (Chapter 11) is also extremely interesting. Pollution by radio-activity is only briefly discussed in Chapter 12, but in 7 pages the authors succeed in giving the layman a coherent and comprehensible account of the main hazards. A final chapter describes the meteorological conditions which determine whether pollution will accumulate or disperse.

Each chapter is followed by a good bibliography.

Taken as a whole this is an extremely helpful manual in which a vast amount of available information is collected together for the benefit of those approaching the problem for the first time. It is to be hoped that Part II, dealing with air pollution control, maintains the high standard it has set. *J. McK. Ellison*

PORT, SHIP AND AVIATION HYGIENE

OTTERLAND, A. **A Sociomedical Study of the Mortality in Merchant Seafarers. Analysis of Deaths in the Population of Active Seafarers registered in Sweden 1945–1954.** *Acta. Med. Scandinavica.* 1960, v. 167, Suppl. 357, 300 pp., illustrated. [Numerous refs.]

This is a very interesting and comprehensive report and the amount of research required to bring it to fruition is shown by the number of tributes paid by the author to various persons, organizations, and authorities, at the end of the preface.

Although he states that he served as a ship's doctor in the Merchant Navy for only a little over two years, he has obviously studied the psychological as well as the physical aspect of seafarers' lives.

Chapter 1. The survey commences by stating that the mortality among seafarers has been high since the beginning of seafaring history; and Table 1 (p. 10) gives some figures from literature on the mortality of seafarers from the year 1227 to 1957. The table indicates that the death rate has gone down steadily, the greatest drops taking place in the middle of the 19th century. This is ascribed to three main reasons—improvement in living conditions, the introduction of vaccination and the discovery of specific bactericidal drugs. In addition, the improvement in shipbuilding, the development of nautical medicine and improved legislation have also played a part.

The number of men engaged in merchant vessels has increased during the centuries but not in proportion to the increase in tonnage. Ships of 400 tons of the old East India Company needed a crew of 150 to 200 men; a modern 10,000-ton vessel only needs about 50 men.

Treatment aboard ship by persons with medical training has been reported from the time of the Vikings. There were ships' doctors in the Swedish Navy in the 15th and 16th centuries. Although a few reports on medical problems, particularly scurvy, were published in the 16th century, it was not until the 18th century that any large publications appeared. Carl Peter THUNBERG, the Swedish physician, published four volumes between 1788 and 1793 describing his journey to Africa, and wrote "One hundred and fifty men lay sick nearly the whole time until we crossed the Equator and the weakest of them—136 men—had died off". The ordinary ship's company was about 150 men but probably a much larger number of men had been shipped

when the voyage began. Eleven diseases, headed by spotted fever, are listed as the cause of the deaths.

Christian THAM (1720–1782) who was employed as a supercargo in various Swedish ships travelling to China between the years 1740 and 1742, confirmed in his notes that men were lost mainly because of scurvy and infection, as well as by accidents and drowning. Similar results were also found in the Swedish Navy at that time. Scurvy was the disease which took the largest toll, and the results of investigations by LIND on the value of lemon juice as an antiscorbutic agent were published in 1753. The commonest causes of death at that time were fevers, consumptions, smallpox, fluxes and scurvy. Similar reports were issued during this period, notably by BLANE (1749–1834), FAXE (1733–1793) and TROTTER (1797). Reports then died down until the first Decennial Supplements on Occupational Mortality published by the Registrar General of England in 1851.

G. J. CARR in "Health Problems in the Merchant Navy" (*Brit. J. Indust. Med.*, 1945, v. 2, 65) compared the death rates among seamen with those in a number of other occupations, and comments "the sea as a calling is the most hazardous of all large group activities except perhaps that of the soldier on active service".

In 1911 the Swedish Board of Trade carried out a statistical investigation of the occupation of seamen. The results were published in two volumes, the first in 1915 and the second in 1919. Since these publications, the Swedish Board of Shipping and Navigation has issued a yearly analysis of accidents among seafarers. It is obvious from these reports that seafaring is an extremely hazardous occupation, especially as regards the severity of accidents.

Chapter 2 deals with the "Influence of International Conventions and Agreements on Development of Social Medicine in the Merchant Navies".

The social legislation consists of provisions in the Merchant Seamen Act, 1953, and deals with employment contracts, medical care, vacations, discipline, etc.: also belonging to social legislation are the Seamen's Hours of Work Act, Housing Proclamation, Food Regulations and Statutory Orders concerning Medical Supplies on board ship. Other Acts cover seamen against disease and occupational accidents.

The Merchant Seamen Act, 1935, makes it obligatory for the seamen to undergo medical examination if the master so orders. The Act also lays down the procedures to be undertaken by the master should a seaman be taken ill or sustain injury either at sea or in port.

In the event of a seaman dying on board, the master has to follow a certain set of regulations.

Chapter 3 enumerates the sources of data of this investigation and covers the period 1945–1954.

The duties of a master under the Swedish Maritime Law in the event of anyone aboard dying, or sustaining serious injury, or serious epidemics, are described in detail.

Since 1954 every seafarer must have certificates attesting that he has undergone fluoroscopic examination, Wassermann testing and tuberculin testing. He must have a certain degree of acuity in vision and hearing and not be diseased, disabled or injured to an extent that makes it impossible to carry out his work.

Table 21 shows the deaths among merchant seafarers registered in Sweden between 1945 and 1954, analysed by sources of information regarding death and causes of death, and Table 23 gives the deaths among seafarers not reported to the National Board of Shipping and Navigation in compliance with Act 40 of the Swedish Maritime Law.

Chapter 4 describes the examination of census returns and the registers of the four seafarers' unions in order to establish the total number of Swedish active seafarers registered between 1945 and 1954.

Chapter 5 shows how the recorded deaths were checked and the elimination of any persons who proved not to be seafarers on active service, such as ships' passengers or fishermen. The methods adopted to sift the various sources of information, both primary and supplementary, are described in detail, and the number of cases registered as deaths among seafarers and not included in the series is given in Table 27.

Chapter 6 discusses the classification of causes of death and points out that the officially recorded cause of death did not always correspond with the cause that appeared from other documents; it was therefore decided to reclassify such cases in accordance with the Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death (Geneva, 1957).

Chapter 7 describes the statistical methods used in the present survey.

Chapter 8 discusses the main social features among seafarers, and it is pointed out that men moved from the country into the towns and from north Sweden to south Sweden.

Chapter 9 deals with the main traits in the mortality of the studied seafarers and points out that vital statistics have been in existence in Sweden since 1749. It is deduced that the death rate among active seafarers was more than 100% higher than among all Swedish males of the same ages. Also that the death rate among ratings was considerably higher than among officers.

The age-specific death rates for different causes of death in Swedish males aged 15 to 69 were calculated and shown in Table 70 (p. 202), and the causes discussed. Although tuberculosis has decreased both in incidence and mortality, there is still a high incidence of fatal tuberculosis among seafarers. The necessity for intensifying preventive measures is borne out by the fact that the 20,000 roentgenographic examinations of the lungs revealed 167 cases of tuberculosis. Table 71 (p. 204) shows that the mortality from tuberculosis among seafarers was similar to that in the standard population. In order to see whether there was the same decrease in deaths from tuberculosis among seafarers as there was among the rest of the population, the periods 1945–1950 and 1951–1954 were studied separately and the results given in Table 72 (p. 205).

It has always been accepted that seafarers were much more apt than others to contract venereal disease, and in World War I the large increase in the number of cases led to the Brussels Convention of 1924 and an international agreement to give seafarers free treatment for these diseases. Numerous reports on the incidence of these diseases have been published and the importance of providing adequate treatment aboard merchant ships has been stressed by several authors.

Malaria was given as a common cause of death among seafarers as far back as the 18th century. Antimalarial treatment is still considered to be important for seafarers and the disease is still a problem in this occupation.

Analysing the results given in Table 72 it is stated that the seafarers of this period showed a high mortality from syphilis, malaria and infective diseases other than tuberculosis, and that the mortality did not decrease at the same rate as it did among Swedish males aged 15 to 69. Living quarters aboard where men are forced into constant and close contact is one reason attributed to high mortality from infective diseases, and a number of suggestions for improving health conditions generally among seamen are enumerated.

Deaths due to circulatory disease form the second largest group of medical deaths among seafarers. Analysis of the figures for the various departments showed that the mortality was slightly lower for the deck and engine room than for the catering personnel, and the officers showed a greater mortality than the ratings. The causative factors are discussed and also the question of fitness for work at sea.

Diseases of the digestive system have always been considered prevalent among seafarers. The causes for the high mortality are attributed to two main causes—the inability to get proper medical treatment in the event of an emergency such as haemorrhage from gastric ulcer, and addiction to alcohol.

The great number of accidents fatal and otherwise has been emphasized for many years. An analysis of accidents among Swedish seafarers in 1957 is given in Appendix A3. Appendix A1 and Appendix A2 taken from the reports of the Board of Shipping and Navigation, and the National Insurance Office, respectively, show the number of accidents among seafarers.

In *Chapter 10* it is pointed out that the present investigation showed that mortality among seafarers differed distinctly from that among Swedish males of the same age. These differences are attributed to the occupational environment aboard ship, the socio-medical environment peculiar to seafaring, as well as socio-medical features prevailing among the categories from which seafarers are recruited. Mortality is also influenced by pre-occupational health. Examples of men having signed on although suffering from some form of disease are given and it is suggested that these factors might also affect the mortality from accidents.

There are 12½ pages of references and the index is given at the end. *Edward R. Peirce*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

Nelson, I. D. M. & Morse, R. J. **A Pilot Study of Office Accommodation.** *Med. Officer.* 1960, Sept. 9, v. 104, No. 11, 163–5.

The survey described here was concerned only with offices as defined in the Gowers Report [this *Bulletin,* 1949, v. 24, 765] and was carried out in Barrow-in-Furness on a random sample of 50 offices or suites of offices accommodating 505 employees. Offices forming part of a factory, workshop or shop were not included.

Data on measurements of rooms, window size, temperature and light intensity were obtained by personal visits, when the premises were inspected and particulars obtained from the principal or office manager. The findings are described in some detail and although the state of the buildings were generally satisfactory a considerable number of inadequacies and imperfections were found. Among defects found were that only 15 offices provided hand towels though washing facilities were generally reasonable; in 22 offices there were no first-aid arrangements; in 21 there were no fire precautions, facilities for drying clothes were most inadequate and seats supplied for office workers were of poor standard.

The conclusions drawn from this small pilot survey are: (1) all offices visited were grateful for advice, (2) smaller towns have different problems from large cities, and (3) it would appear that standards are better, as found in this survey, than in reported standards from large cities. *M. E. Delafield*

Hickish, D. E. & Challen, P. J. R. **A Study of Noise in a Circular-Saw Shop and its Effect on Hearing.** *Ann. Occup. Hyg.* London. 1960, July, v. 2, No. 2, 133–40, 7 figs. (2 on pl.)

In this paper there is an account of the investigation of a noise problem in one of the member firms of the Slough Industrial Health Service. The problem arises in the workshop where 3 types of saw blade are used—ripsaw, "novelty" and planing blades.

Tape recordings of the noise from each of these types of blade were made and Octave Band analyses of the noise were carried out. Clinical investigation was then made—a preliminary study on a subject exposed to noise for 3 hours (one of the authors of this paper) and later on 4 men exposed to the noise of a saw in their work. The hearing of the men was tested on a Monday morning and towards the end of their week's work by pure-tone audiometry with an Amplivox Model 61 Audiometer calibrated to British Standard 2497. This testing was repeated at intervals of up to 45 hours after

cessation of exposure to noise. Figures and tables set out the findings of the investigation. It was found that the noise produced during certain circular sawing operations exceeds a recommended damage risk criterion [LITTLER, this *Bulletin,* 1959, v. 34, 1010] at frequencies above 600 cycles/sec. A marked temporary loss of hearing resulted in the experimental subject exposed to the noise for 3 hours. This temporary loss was also demonstrated in the 4 workers in addition to "a permanent loss in excess of that considered to be due to ageing".

There is some discussion of the solution of the problem of the noisy circular saw which is not an easy one. *M. E. Delafield*

ERMISCH, W., HAYDN, G. & WITTGENS, H. Lärmschäden und Lärmschutz. Erfahrungen bei 2415 Lärmarbeitern der Deutschen Bundesbahn. [**Noise —its Effects and their Prevention. Experiences of 2,415 Railway Workers exposed to Noise**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 2, 120–58, 25 figs. [44 refs.]

A considerable number of references to published work on the effects of noise of different intensities and characters are here reviewed to introduce the results of the investigation of 2,415 railway workers exposed to noise. These results were analysed and statistically examined in relation to intensity of the noise in different sorts of work, and the extent of hearing loss by age of worker and his years of exposure to noise. An estimate is made of the proportion of the measured hearing loss that may be attributed to exposure to noise by comparison of the findings in these workers with those obtained as average in other workers which show the well-known ageing effect on acuity of hearing.

There is a detailed description with many figures of the results of the investigation, which confirm the observations of other workers on the effects of noise on hearing. The prevention of these hearing losses is discussed with stress on the importance of medical supervision and mention is made also of the need for further work on the possibility that long exposure to noise may bring about the systemic effect of premature ageing of the worker. *M. E. Delafield*

KETTNER, H. Neue MAK (Maximale Arbeitsplatz-Konzentrationen) in der Sowjet-Union. [**New Maximum Allowable Concentration Levels in Industry in the Soviet Union**] *Staub.* Düsseldorf. 1960, Oct. 1, v. 20, No. 10, 369–70.

HRUBÝ, S., MARATKA, Z., NAUS, A. & PIHRT, J. Některé zdravotnické problémy spojené se zpracováním a používáním koření. [**Some Health Problems involved in the processing and use of Spices**] *Časopis Lékařů Českých.* Prague. 1960, Sept. 30, v. 99, No. 40, 1261–6. English summary.

The English summary appended to the paper is as follows:—

"The authors examined a group of people engaged in grinding and packing spices and tried to ascertain the influence exerted by processing of spices, which is associated with a considerable dispersal of small particles of the spices in the atmosphere of the workshop, on the health of the employees. The condition of the gastric mucosa in the individuals examined, no matter whether they suffered from subjective complaints or not, bore signs of superficial irritation or inflammation.

"Most spices are infested with moulds and their spores penetrate together with dust particles into the atmosphere. The authors found a marked correlation between the frequent incidence of moulds and the incidence of greyish-white coatings in the oral cavity. Changes of the nasal mucosa correspond to the non-specific changes produced by other inert dusts. The hyposmia caused by the transitional changes of the mucosa and the exhaustion of smell perception is restored before the next shift.

"The authors assume that spices have a generally irritant effect on the gastric mucosa and conclude that excessive use of spices in the diet has also an unfavourable effect on people with a more sensitive or even affected digestive system. The moulds found on the spices have an adverse effect on the condition of the mucosa and can be transmitted with the spices to the foodstuffs."

BLÜMLEIN, H. Berufliche Wärmestrahlenbelastung und chronische Schleimhautentzündung der oberen Luftwege. [**Chronic Disorders of the Upper Respiratory Tract in Workers exposed to Heat Radiation**] *Arch. f. Hyg. u. Bakt.* 1960, Aug., v. 144, No. 6, 462–6.

In this paper there is an account of the results of medical examinations of 343 industrial workers classified in 4 different groups according to occupation: (1) exposed to heat without dust (177 men), (2) heat and dust (42), (3) dust but no heat radiation (24), and (4) a control group (100) exposed neither to heat nor dust.

There is a description with tables of the frequency in each of the 4 groups of (1) symptoms such as headache, nasal obstruction, dryness of nose and throat and frequent nose bleeding, and (2) objective findings such as chronic rhinitis, pharyngitis, laryngitis and sinusitis.

The main finding was that exposure to heat radiation caused chronic inflammation of the mucosa in the upper respiratory tract, particularly in iron-works and glass-works and mostly among those occupied at certain defined places in the factory.

These effects of heat should be considered in any revision of legislation in occupational disease.

[See also this *Bulletin,* 1959, v. 34, 1012, *bis*; 1960, v. 35, 752.] *M. E. Delafield*

BRUUSGAARD, A. Astmalignende sykdom blant Norske aluminiumarbeidere. [**Asthma-like Disease among Norwegian Aluminium Workers**] *Tidskr.f.d. Norske Laegeforening.* 1960, Sept. 1, v. 80, No. 17, 796–7. English summary.

Cases of asthma-like disease having been reported in workers employed in the furnaces of factories engaged in the electrolytic production of aluminium from its oxide, all the factories of this kind in Norway were requested in 1954 to collect all the data pertinent to this

problem. So far only 3 such factories have complied satisfactorily with this injunction, and it is with their returns that Bruusgaard is concerned in the present report. In his first table he presents 709 workers occupied or previously occupied (having moved on to other work in the same factory) in furnaces. Among these 709 were 29 asthmatics—an asthma rate of 4·1%. Among the 1,032 workers employed in these 3 factories, but not in their furnaces, there were 8 cases of asthma or an asthma rate of 0·8%. The same table classes the workers in 10-year age-groups beginning with all under 25 years. In the age-group 55–64 years there were 73 men engaged or previously engaged in the furnaces. Among them were 11 asthmatics—an asthma rate of 15%. In the same age-group there were 122 "non-furnace" workers, and among them were 2 asthmatics (1·6%).

Bruusgaard's second table has to do with a district in which a factory has only just begun to produce aluminium. To provide data wherewith to compare this district's asthma rate after the factory has been at work for some time, the asthma rate for the last 4 years in 1,834 insured male workers is quoted. Here, too, the workers are classed in 10-year age-groups. The total or average asthma rate was 0·78%. *Claude Lillingston*

SEXTON, R. J.; WEIL, C. S.; CONDRA, Naomi I.; KETCHAM, N. H.; NORTON, R. W. **The Hazards to Health in the Hydrogenation of Coal. I. An Introductory Statement on General Information, Process Description, and a Definition of the Problem** [SEXTON]. *Arch. Environment. Health.* Chicago. 1960, Sept., v. 1, No. 3, 181–6, 6 figs. [11 refs.] **II. Carcinogenic Effect of Materials on the Skin of Mice** [WEIL & CONDRA]. *Ibid.*, 187–93, 1 fig. [15 refs.] **III. The Industrial Hygiene Studies** [KETCHAM & NORTON]. *Ibid.*, 194–207, 9 figs. **IV. The Control Program and the Clinical Effects** [SEXTON]. *Ibid.*, 208–31, 12 figs. [47 refs.]

[This series of 4 papers were read at the Twelfth Annual Meeting of the American Academy of Occupational Medicine, Williamsburg, Va., February 12, 1960. They relate to a single project and so should be read as a whole.]

I. The raw material used in the coal hydrogenation process is bituminous coal, which is a macromolecule hydrocarbon. In 1913 in Germany BERGIUS showed that coal when treated with hydrogen at high pressures and temperatures yielded 85% of its weight in soluble liquid products consisting of phenolic substances and hydrocarbons similar to the petroleum hydrocarbons. The first commercial coal hydrogenation plant was built at Leuna, Germany, in 1926 and during World War II the 12 plants, which by then had been developed, supplied approximately 85% of the aviation fuel used by the Luftwaffe. These plants did not produce chemicals.

In 1952, after 17 years of research, engineering and the operation of laboratory-sized plants, the first large-scale pilot plant production of chemicals from coal hydrogenation began at Institute, Williamsburg, Va.

The coal hydrogenation process from the preparation of the coal paste to the final products is described and copiously illustrated by pictures of the various units of the plant and diagrams of the line flow. The resultant aromatic and aliphatic chemicals and the acidic (phenolic) and basic (nitrogen bases) fractions are tabulated. As many of these products have been identified as toxic, some carcinogenic, to workmen the next stage was to undertake laboratory studies.

II. The second paper describes the laboratory investigations which were carried out with various fractions produced in the line process to discover whether or not they were carcinogenic. A suitably controlled experiment was designed. Mice were used and the shaved skin was painted with the substances under investigation. Tests were made to assess the protective value of barrier substances and washing with soap and water. The results of the various experiments are recorded and tabulated. The light and heavy oil products proved mildly tumour-producing except that the light oil fraction boiling below 260°C. and its derivatives had no such power. The streams boiling at higher temperatures, middle oil, light oil stream residue, pasting oil and pitch product were all highly carcinogenic. Barrier substances and various wash methods only slightly delayed tumour induction period.

III. From the laboratory the investigations were extended to the plant. The object was to discover the processes and areas of the working environment, where workmen might be exposed to carcinogenic oils. This is the subject of the third paper. It was observed that skin contamination was by direct contact or indirectly from air-borne fumes, dusts and droplets. As a result of the hygiene studies the team were enabled to recommend preventive measures, including alterations to the plant and operating procedures. Protective clothing and personal hygiene were underlined as a first line of defence.

IV. Dr. R. Sexton in the final paper describes in detail the medical supervision of the workers in the plant. Considerable reliance was placed on an unremitting programme of health education [this merits careful study]. A very thorough system of periodical skin inspection was arranged. The following is worthy of quotation:

"The workers are *completely nude* [italics inserted] during the skin inspections, and all abnormalities are recorded on a body outline form [figures illustrated] developed specifically for this project."

[Scientifically this enquiry adds little, if anything, to what is already well established. It is, however, worthy of close study because of its practical approach to the problems of a new plant. First of all based on existing knowledge it was anticipated that hazards would probably arise. These were studied at the pilot stage. At the working stage the engineers following environmental studies were enabled to apply methods of control, the effectiveness of which were constantly tested and advanced by intensive medical supervision. The health education programme is a model and one is particularly impressed by the frankness with which the workmen are informed of the risks and so encouraged to co-operate intelligently in the preventive programme.]

A. Meiklejohn

OCCUPATIONAL DISEASES

DAWES, J. G. & MAGUIRE, B. A. **The Thermal Precipitator and the P.R.U. Handpump: a Critical Study.** (With appendices by D. T. O'CONNOR & D. L. TYE.) *Safety in Mines Research Establishment.* [Portobello St., Sheffield, 1.] *Research Rept.* No. 187. 1960, Apr., 64 mimeographed pp., 48 figs. [30 refs.] [5s. 6d.]

The thermal precipitator is the reference instrument used in British coal mines for the determination of concentrations of airborne dust. It is sometimes necessary to use other instruments to measure dust concentrations, and when this is done, *e.g.*, with the PRU hand pump, the attempt is made to convert the measurements to equivalent thermal-precipitator values. Simultaneous measurements by the thermal precipitator and by another instrument are sometimes made in a given dust cloud, with the object of calibrating the second instrument in terms of the thermal precipitator, and when variations occur in the relation connecting the two instruments the errors are frequently assigned to the second instrument—it is assumed that the thermal-precipitator measurements are accurate.

In the present paper the errors that may arise with the thermal precipitator are examined, and these are compared with the errors that arise in handpump measurements of dust concentration. Only a small number of instruments have been tested, and no attempt is made to generalize about the magnitude of the errors that occur. The instruments that were used were in normal condition. Only the variations that occurred when samples were taken by the two instruments in the same dust cloud are examined.

If the concentration derived from the thermal precipitator is to be accurate 4 basic conditions must be satisfied. All the particles in the appropriate size range that are present in the volume of the dust cloud that is sampled must be deposited in the instrument; there must be no overlap of particles on the collecting surfaces of the glass slips; there must be no errors in deciding whether an observed particle lies in the standard range of sizes; and the deposition of particles must be uniform over the lengths of the deposits on the two glass slips. There may be considerable differences between the counts made by different observers on the same sample. Thus, instrumental and personal factors may together cause substantial errors. It is remarked that in practice 2 experienced observers, using 2 nominally identical thermal precipitators properly maintained, when sampling in the same dust cloud underground can produce estimates of dust concentration which vary by as much as 50%.

It is concluded that in a given dust cloud the consistency of measurements with the handpump is appreciably greater than can be obtained with the thermal precipitator.

The appendices describe the techniques for evaluating dust concentrations with the thermal precipitator and with the PRU handpump. *Thomas Bedford*

SHERWOOD, R. J. & GREENHALGH, D. M. S. **A Personal Air Sampler.** *Ann. Occup. Hyg.* London. 1960, July, v. 2, No. 2, 127–32, 5 figs. (2 on 2 pls.) [13 refs.]

This sampler can be carried unobtrusively by a workman and indicates the average concentration of atmospheric contaminant to which he has been exposed during his activities over a period of a day or longer. It performs a function analogous to that of the film badge for measuring exposure to X-radiation.

An electric motor, operated by mercury batteries having an operational life of 30 or 100 hours, drives a diaphragm pump at constant speed. The air flow depends on the resistance of the filter paper through which the pump aspirates and is shown on a graph that also indicates the electric power consumption. The pump has a high mechanical efficiency obtained by the use of a Fluon (polytetrafluoroethylene) diaphragm, valves made of aluminized Melinex film and a Teflon eccentric.

The 30-hour model, which goes into an ordinary bicycle lamp case and weighs 1 lb., can be carried in the pocket. The 100-hour model, incorporating an electric clock to indicate the total flow, weighs 2 lb. and can be worn in a pouch attached to a belt. Experience with these samplers in estimating radioactive dust is described; it is suggested that they could be used for toxic vapours with silica gel or other absorbents in place of filter paper. *C. N. Davies*

STAUB. Düsseldorf. 1960, Aug. 1, v. 20, No. 8, 241–324, numerous figs. [Numerous refs.] Berichtsausgabe über die Gemeinschaftstagung "Entwicklungstendenzen des Staubmesswesens" 4. bis 6. Mai 1960 in Wien. **[Trends of Development in Dust Measurement]**

The full text of papers and discussion at a conference in Vienna, May 4–6, 1960, organized by the German Engineers' Association Dust Section, the Austrian Engineers' and Architects' Association and the Austrian Centre for Silicotic-dust Prevention, is given in this issue of *Staub*.

Section 1: Measurement of Dust Concentration

In *The state of dust-measurement technique* (pp. 243–244), P. NOSS gives general introductory remarks, with special reference to current German methods and the tendency to recording instruments.

In *Dust deposition by thermal and pressure diffusion* (pp. 244–252), G. STETTER outlines the theory concerning the force experienced by a dust particle due to unequal molecular bombardment of its opposite sides in a temperature or pressure gradient. The thermal effect is widely applied in dust-sampling instruments but is unlikely to be of use in cleaning large volumes of air, except perhaps in highly turbulent gas streams with an appreciable temperature-gradient at the boundary layer. The pressure effect is difficult to apply since it occurs only in flowing gases and the dust transport is annulled

by the return flow of the air; but it is of academic interest because of its analogy to the thermal effect.

In *Studies on the precision of particle-size analysis* (pp. 253–266), H. RUMPF discusses the different particle parameters (area, volume, diameter, falling-speed, density, composition), the various possible presentations of size-distribution results, and the effect on these parameters of the errors in sieve and sedimentation analysis.

T. GAST, *Indicating and recording gravimetric dust-measuring instruments* (pp. 266–272). These are dust balances in which a small fan draws air through an electrostatic precipitator. Periodically the deposit is weighed by a servo torsion balance, the weight recorded, the deposit cleaned off, and sampling resumed. For different places and dust concentrations, three such balances have been made. One, using transistors, is only 15 inches long, weighs 20 lb. including batteries giving 24 hours' operation, and is safe for use in gassy coal-mines.

The discussion (pp. 273–274) covers errors in sedimentation analysis due to balances and to effects in the dispersing medium; and the falling speeds of non-spherical particles.

Section 2: Measurement of Dust Deposition

K. SCHWARZ, *Review of problems of dust-deposition measurement* (pp. 275–278). German regulations taking effect in June 1960 require maximum permissible values of air pollution to be determined. This presupposes the availability of reliable instruments. Airborne dust concentration can be more conveniently estimated from measurements of dust deposition than by direct measurement. Funnel deposit gauges and adhesive foils are favoured. M. DIEM in *Measurements of dust deposition* (pp. 278–282), reports results in the first year of a comparative trial of different deposition instruments: all the types had a reproducibility of about ± 20% and agreed reasonably well with each other. The first correlations of deposition rate with airborne concentration measurements, made on the ground and at heights up to 200 ft., are presented.

Practical results of dust-deposition measurements, by A. HELLER (pp. 282–285), describes the measurement of soluble and insoluble materials washed out of the atmosphere by rain, and some routine results are given.

The discussion (p. 285) is concerned with the difficulty of deciding on maximum permissible dust concentrations; and of deducing airborne concentration from deposition measurements of industrial dusts.

Section 3: Organization of Dust Measurement

The work and aims of the Austrian Silicotic-Dust Prevention Centre are described by F. MARESCH (pp. 285–286). The Centre, recently established with headquarters in Vienna and laboratories 100 miles away in Loeben, is an association to which all interested organizations may belong, and is aided scientifically by the 1st Physical Institute of Vienna University. As a first step towards the application of dust-prevention measures, especially in the mining, granite and foundry industries, an organization for routine dust measurement has been set up.

W. KITZLER, *Routine dust monitoring* (pp. 286–289). The konimeter (usually the Sartorius HS standard type, occasionally the mining type) is used in the Austrian Centre's dust measurements because of its simplicity in use and the psychological effectiveness of an immediate, demonstrable dust sample. All particles visible are counted under dark-field illumination. A filter apparatus takes samples for compositional analysis.

H. BREUER, *Dust-measurement in coal-mines* (pp. 290–299). In German mines a photometric estimate of dust composition in konimeter samples is combined with a concentration measurement by tyndalloscope to classify working places in one of four dust levels. To supplement these routine measurements a "fine-dust filter apparatus" has been developed, in which a cyclone collects the coarse, non-respirable dust and a membrane filter the fine fraction. A recording tyndalloscope is also under development. The calibration of instruments, the strategy of routine sampling, and the presentation of results, are also described.

In *Methods of measurement in powder metallurgy* (pp. 299–302), K. TORKAR describes techniques for measurement of particle size, area, and activity of powders, which may also be relevant for analysis of dust samples. A. GOETZ (pp. 303–308), deals with *The origin, properties and determination of the sub-micron aerosols in smogs.* Uncombusted hydrocarbons, NO_2 and SO_2 from industry and automobiles accumulate in stagnant air and interact in sunlight, the products condensing on natural aerosols to build smog particles of about 0·1 micron which reduce visibility and penetrate to the sensitive regions of the lung. Hence physiological response correlates better with the turbidity than with the gaseous concentration of the atmosphere. Eventually the aerosols disappear by further oxidation. An aerosol spectrometer for the study of these aerosols is described.

H. KOCH (pp. 308–310), writes on *Average concentrations and MA levels.* Airborne dust concentration in a working place varies with time both within and between shifts, especially when the ventilation is affected by external temperature and wind. Also the breathing rate of the worker, and hence the dust intake, varies with the work. These factors must be allowed for in comparing measurements taken on one day with the tables of maximum permissible average (MAC) values for exposure over long periods.

In the discussion (pp. 311–312), Prof. A. GOETZ says that since olefines contribute especially to smog formation, their content in automobile fuels in Los Angeles is already restricted to 20%, and ultimately in future to 10%. The aromatic compounds more usual in European fuels are less harmful. Two speakers describe routine dust measurements and suppression techniques in Hungarian coal mines.

Section 4: Measurement of Radio-active Dusts

In a *Review of the problems of measuring radio-active dusts* by J. A. SCHEDLING (p. 313), the problems of sampling and measurement, of correcting for background and absorption, and of analysing radiation-spectrometer measurements, are outlined.

In *Apparatus for the measurement of radio-active dusts in working places* by D. HASENCLEVER (pp. 314–319), a description is given of various routine sampling and radiation-measuring instruments and of the analysis of results, with special reference to the use of open proportional-counters for the evaluation of dust samples on high-efficiency filters.

G. SCHUMANN, *Radio-active pollution of the atmosphere* (pp. 319–324). Natural radio-active contamination of the atmosphere arises chiefly from radon and thoron and decay products from the earth's crust, and only slightly from cosmic rays. Although nuclear weapons have only raised the total activity of the atmosphere by 1%, man-made activity is usually atomic, not gaseous, and so deposits readily, for example on atmospheric aerosols. Activity observations show the life of these aerosols to be about 1 month; and that there is an annual variation in the air exchange between troposphere and stratosphere. Nuclear weapons have increased the carbon 14 content of the atmosphere by 30%, the tritium content by 100 times.

There is no report of a discussion on these 3 papers.

J. R. Hodkinson

RHODESIA, NORTHERN. Ministry of Labour & Mines. The Pneumoconiosis Medical and Research Bureau [PAUL, R., Director] & the Pneumoconiosis Compensation Board [DONNELLY, W. J., Chairman]. **Annual Reports for the Year 1959 with the Pneumoconiosis Compensation Board Balance Sheet as at 31st Dec., 1959 and the Pneumoconiosis Compensation Fund Account for the Year ended 31st Dec., 1959.** 26 pp., 1 fig. 1960. Lusaka: Govt. Printer. [2s.]

[After confirmation of the occurrence of cases of silicosis among copper miners and labourers in the territory the Northern Rhodesia Government in 1944 made temporary arrangements providing for medical examinations and certificates of compensation. These arrangements suitably amended were made permanent in 1949 (this *Bulletin*, 1951, v. 26, 783). A handsome well-equipped Silicosis Medical Bureau—now The Pneumoconiosis Medical and Research Bureau—was opened at Kitwe in March, 1950. Dr. R. PAUL, now director, was then the medical specialist. Under his capable and enthusiastic direction the Bureau, originally modelled on the South African Silicosis Medical Bureau at Johannesburg, has become probably the leading organization of its kind in the world. The Bureau at Kitwe is the centre for completion of initial, periodical and final examinations. In 1957 it was found necessary to provide a subsidiary examination centre in Broken Hill. Unlike bureaux elsewhere it is comprehensive and comprises clinical, radiological, physiological, biochemical, bacteriological (including parasitology) pathological and statistical departments. In conjunction with the Mines Inspectorate located on the same site there is an occupational hygiene unit. The work has not been confined to routine duties but has embraced fundamental and field research. Through the co-operation of the Chamber of Mines smooth operation has been facilitated by conducting the medical examinations at this single centre and not at the separate mines with the exception of Broken Hill Mine which is too remote. Basically the medical arrangements for Europeans and Africans are identical. The average number of Europeans employed underground during 1959 was 2,779 and Africans, 19,566 (Northern Rhodesia Chamber of Mines Year Book, 1959, Kitwe, Northern Rhodesia).]

During 1959 the total number of persons examined amounted to 38,873 (Europeans 6,231; Africans 32,642) involving 40,249 examinations. 99 necropsies were made. First certifications of compensable disease, pneumoconiosis, tuberculosis, and pneumoconiosis with tuberculosis, numbered 62 but of these only 43 had Northern Rhodesia service only (Europeans 4; Africans 39).

First Certifications (Northern Rhodesia service only)

First certifications of persons whose only known exposure to risk of pneumoconiosis has been in Northern Rhodesia mines ...	43
Pneumoconiosis alone (Europeans 2, Africans 15)	17
Pneumoconiosis with tuberculosis (Europeans nil; Africans 6)	6
Tuberculosis alone (Europeans 2; Africans 18)	20
	Mths.
Average length of mining service of the fifteen new (1959) African pneumoconiotics with known exposure to risk in Northern Rhodesia mines	162·5
Average length of mining service of the two new (1959) European pneumoconiotics with known exposure to risk in Northern Rhodesia scheduled mines	193

At initial—pre-employment—examination 10% Europeans and 5% Africans were rejected. [Labour turnover among Africans—largely due to native customs—approximates to 100% per annum.]

Since the discovery of silicosis—now pneumoconiosis—in Northern Rhodesia it had been observed that the incidence of cases certified at the Mufulira mine was substantially higher than at the others. To help elucidate the situation at this mine a special investigation was carried out and is now reported. The following are the conclusions:

"35. Mufulira Mine would be expected to produce a greater number of cases of pneumoconiosis per thousand of exposed population than any other one mine in the Copperbelt, because it has the highest percentage of free silica particles of respirable size in the atmosphere, and because it has a higher labour retention rate and consequently the greatest number of men with the longest dust exposure.

"36. The disproportion in the certification rate between Mufulira and any of the other mines on the Copperbelt is due mainly to the dust conditions that pertained at Mufulira prior to 1950.

"37. There has been a marked improvement in dust conditions at Mufulira, and no case of pneumoconiosis has been certified in any miner employed since 1950 in any of the mines on the Copperbelt including Mufulira, and it is anticipated as a result that there will not be the marked disproportion in certifications as has pertained in previous years under present conditions."

At the end of the year the medical staff consisted of the director, deputy director and 7 other doctors and specialists. There are 5 vacancies owing to difficulties in recruiting medical officers. [It is to be hoped that this state will not persist for it must soon handicap the Bureau in maintaining its outstanding work.]

A. Meiklejohn

CATHCART, R. T., THEODOS, P. A. & FRAIMOW, W. **Anthracosilicosis. Selected Aspects related to the Evaluation of Disability, Cavitation, and the Unusual X-ray.** *Arch. Intern. Med.* 1960, Sept., v. 106, No. 3, 368–77, 7 figs.

Since 1949, 1,690 coalminers from the anthracite coalfields of Pennsylvania have been studied at the Barton Memorial Division, Jefferson Medical College, Philadelphia. All these miners had worked in the mines between 25 and 30 years and with rare exceptions all showed radiographic evidence of anthraco-silicosis [if the photomicrographs in the text are representative of the lung pathology among this group, the designation anthraco-silicosis is accurate; typical whorled silicotic nodules are indisputable.]

The first part of the study concerned the evaluation of pulmonary impairment in relation to the radiographic nature and extent of the disease. In general the greater the degree of silicosis [pneumoconiosis?] the greater was the amount of pulmonary disability. Frequent exceptions were noted in which disability in cases of massive fibrosis in men of the same age varied between no disability and total incapacity for work. Similarly in cases of long exposed men without radiographic signs of pneumoconiosis, pulmonary function was only slightly impaired in some, whereas in others impairment was considerable. This variation is attributed to differences in the degree of pulmonary emphysema. The second part of the study was the investigation of the occurrence of cavitation occurring in areas of massive fibrosis. This was observed in 182 (10·8%) among the 1,690 miners. In 68% of the patients with cavities, single and multiple, the cavitation was due to tuberculosis with positive sputum. After very full investigation 18% of cases with cavities were attributed to ischaemic necrosis, which was manifested clinically by expectoration of copious amounts of black spit. This ischaemic type of cavitation did not appear prognostically to influence the course of the underlying anthraco-silicosis.

Finally attention was directed to those patients whose X-rays were classified as atypical and borderline but not conclusive of pneumoconiosis. Lung biopsy by the Klassen (intercostal) technique was undertaken in 30 cases. In 9 of these the diagnosis of anthraco-silicosis was definitely established histologically (figures 6 and 7). The procedure proved to be simple and safe and so it is submitted that lung biopsy is a useful tool in the diagnosis of doubtful cases.

[This contribution suggests that the dust risks of mining in anthracite mines are not identical in all parts of the world. In South Wales, Great Britain, the pulmonary pathology generally accords with pneumoconiosis of coalworkers—simple and complicated—which in present context might be named anthracosis. By contrast in anthracite miners in Pennsylvania the pathological and histological changes represent anthraco-silicosis.] *A. Meiklejohn*

PROYARD, G. Le danger des poussières provoquées par le sciage des briques. [**Dust Hazard Arising out of Brick Sawing**] *Arch. Malad. Professionnelles.* Paris. 1960, July–Aug., v. 21, Nos. 7–8, 428–31.

The traditional method of cutting and dressing bricks to size and shape is by hammer and chisel. In recent years in the building and repair of furnaces there has been a great increase in the use of portable carborundum saws for cutting refractory brick linings. The operation is very dusty and with some types of refractory materials the dust is highly dangerous owing to the presence of cristobalite, tridymite and quartz particles of respirable size. The number of men at risk is small, and so adverse effects on workmen may be sporadic and therefore overlooked. 2 definite cases of rapidly forming silicosis were observed among such a small team of men. The situation called urgently for preventive measures. Amelioration of the dusty conditions was achieved by the use of respirators, local exhaust ventilation and the application of a wetting agent—ORZAN—a by-product of the wood-pulp industry.

[This is just another experience—not new—which emphasizes how important it is for physicians not only to ascertain accurately the employment history but to enquire closely into the working processes and materials. An analogous practice has developed in recent years in Great Britain, namely, the cleaning of the stonework of monumental buildings by means of power-driven portable carborundum disc grinders. The practice demands urgent measures by the Factory Inspectorate for the protection of the workmen.] *A. Meiklejohn*

FONTANELLA, E., MAGRÌ, G. & PACCAGNELLA, B. l'inquinamento atmosferico da polveri di cementificio. Rilievi diretti e considerazioni. [**Atmospheric Pollution from Cement Factories Dust. Direct Analyses and Considerations**] *Igiene Moderna.* 1960, v. 53, Nos. 1/4, 67–86, 1 fig. [14 refs.] English summary.

After pointing out that, while it is difficult to get any direct evidence of injury to health near a cement works, the contamination of the atmosphere is all too evident, the authors describe an investigation made in an area close to a small cement works in the Piave valley of Northern Italy from July to November 1958.

The works were situated up-wind of a small town, measures to reduce contamination were by no means satisfactory, and dust, etc. could be seen everywhere where the investigations were carried out. The aims were to ascertain (a) the amount of dust emitted; (b) the average atmospheric contamination by substances settling on areas near the works; (c) amounts of suspended particles in the same areas. For (a) the materials were collected on filter paper, for (b) standard deposit meters were located at various sites and distances from the works; (c) the Owens konimeter was used, counting being done by the phase-contrast microscope at × 1,000 diameters. The usual direction of the wind was from the north down the valley, so 2 sites to the south and 1 to the north of the works were selected. Samples for the Owens konimeter were taken at various times of the day and under varying meteorological conditions.

The results showed that for (a) about 100 tons a month were emitted not including the dust from activities below smokestack levels especially that caused by putting the final product into sacks; for (b) the amounts were 5–10 times greater than for a similar investigation

at the city of Padua. The amount of total SiO_2 varied from 12 to 15%, and free Si 3 to 5%. By the Owens konimeter over 17,000 particles per litre of air were found at 2 km. down-wind, rising to over 500,000 per litre 100 m. from the works, while 800 metres up-wind the average was 7,500 per litre. The majority of the particles were less than 2μ.

The authors point out that the *p*H of the deposit was noticeably on the alkaline side [which may point to an explanation of the asthmatic attacks alleged to have been experienced by certain residents near cement works in England], while the size of the particles and the very considerable quantities together with the free Si content are such as to give rise to apprehension as to their effect on public health. Although their investigations were carried out in an area which, except near the works, is almost uninhabited, the risks in a populous area cannot be negligible even though all possible steps are taken to minimize them.

They comment on the risks to the operatives themselves, for in 6 years, out of 200 operatives, there have been 66 cases of silicosis, and 53 of dermatitis.

W. K. Dunscombe

MOTLEY, H. L. **Pulmonary Function Studies in Diatomaceous Earth Workers. 2. A Cross Section Survey of 98 Workers on the Job.** *Indust. Med. & Surgery.* Miami. 1960, Aug., v. 29, No. 8, 370–78, 6 figs. [12 refs.]

In 1953–54 the United States Public Health Service [COOPER and CRALLEY, *Pneumoconiosis in Diatomite Mining and Processing*, Pub. Health Service Publication No. 601, Washington, D.C., 1958, U.S. Dept. Health Education and Welfare] carried out a full-scale investigation into pulmonary disease in the diatomite industry. It emerged that when crude diatomaceous earth is heated, crystalline cristobalite is formed from the amorphous silicon dioxide and this is capable of producing disabling pneumoconiosis. The clinical and radiographic features of this pneumoconiosis differ from those of coal-workers' pneumoconiosis. Thus serious disease was observed after so short an exposure as 3–5 years as against 15–25 years, and linear markings on the chest radiograph were a frequent characteristic as opposed to nodulation.

Professor H. L. Motley, director of the Cardio-Respiratory Laboratory, University of Southern California School of Medicine, undertook pulmonary function studies in a group of men chosen from the original Public Health Service enquiry. 150 men were selected to represent a cross-section of the workmen in the industry. For various reasons only 98 of these men submitted themselves for the tests [this invalidates the representative sample].

The battery of tests included measurement of total vital capacity, timed vital capacity for 3 seconds, and maximal breathing capacity All these tests were made before and after administration of a broncho-dilator. Residual air was measured and checked both by the oxygen open circuit and the improved helium closed circuit methods. The oxygen content, oxygen capacity and carbon dioxide content were obtained on resting and exercise samples of arterial blood drawn from the brachial artery. Radiographic appearances were classified according to the scheme adopted in the original clinical survey [this differs from the Sydney International Classification, which was current then].

No correlation was found between the pulmonary function measurements and the radiographic stage of pneumoconiosis. The evidence indicated that disability cannot be accurately assessed from the radiographic appearances and it is accordingly submitted that removal of a worker from the job should not be made on the basis of the X-ray. In support of this it is remarked that although the 6 cases in the study with a severe degree of function impairment had extensive X-ray changes, other workers with similar changes had normal function.

A. Meiklejohn

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication hors-série. Le Coeur pulmonaire chronique dans les pneumoconioses. Importance relative des altérations vasculaires et du déficit ventilatoire dans sa pathogénie [LAVENNE, F., MEERSSEMAN, F., KREMER, R. & BRASSEUR, L.]. **[Cor pulmonale in the Different Varieties of Pneumoconiosis. Relative Importance of Pulmonary Vascular Changes and reduction in Pulmonary Ventilation in its Causation]** Reprinted from *Progrès en Cardiologie.* 1959, v. 2, 306–18, 8 figs. (44 refs.)]

This contribution is almost entirely a review of the international literature on the subject and its real value depends on the list of references. The team, however, have incorporated the results of a study of 27 cases of coalworkers' pneumoconiosis (9 micronodular and 9 early and 9 advanced massive fibrosis). Pulmonary arterial pressure was measured before and after a defined load of exercise (50 watts and 100 watts). Measurements were also made of maximum expiratory volume per second (VEMS=forced expiratory volume per second FEVS) [see this *Bulletin*, 1958, v. 33, 355]. The results confirmed previous researches that there is a correlation between pulmonary hypertension and diminution of maximum breathing capacity, particularly after exercise.

The authors conclude that the physio-pathology of cor pulmonale in *silicosis* (abstracter's italics) is still imperfectly understood and that further research into pulmonary haemodynamics is necessary both in cases of simple and massive pneumoconiosis. This is particularly important in subjects having a VEMS between 1,500 and 2,500 c.c.

[In this article as in many others the reviewer finds it almost impossible to decide when silicosis is used to denote the specific disease due to free crystalline silica and when it is used as synonymous with pneumoconiosis in general. British authors often quite wrongly use pneumoconiosis for coalworkers' pneumoconiosis.]

A. Meiklejohn

PIIPER, J. Die funktionellen Abschnitte des Lungengefässsystems. **[The Functional Aspect of the Pulmonary Vascular System]** *Beiträge z. Silikose-Forschung.* 1960, No. 67, 1–64, 10 figs. [49 refs.]

BYERS, P. D., KING, E. J. & HARRISON, C. V. **The Effect of Triton, a Surface-Active Polyoxyethylene Ether, on the Development of Experimental Silicosis.** *Brit. J. Exper. Path.* 1960, Aug., v. 41, No. 4, 438–42, 3 figs. (2 on pl.)

"On the basis of gross and microscopic pathology, and of collagen analyses, it is concluded that Triton does not have any effect on the course of experimental silicosis produced in rats by intratracheally injected powdered quartz dust."

BRUNO, L. Il rischio di saturnismo tra i lavoratori addetti alle scocche di automobili. **[Lead Poisoning Hazard in Workers employed on Car Bodies]** *Med. d. Lavoro.* 1960, Mar., v. 51, No. 3, 225–31. English summary.

This paper deals with the lead hazard to workers in a car body factory where output has been rapidly increasing since 1955. Production has since been re-organized on the "line" system and emery wheels, revolving brushes and other mechanical aids have replaced such hand operations as filing, soldering and other smoothing and finishing of joints and edges in preparation for paint spraying. The workers employed on these tasks then began to have abdominal complaints, with colic in one case, suggestive of lead poisoning; the older employees seemed to have acquired some degree of tolerance and remained free from any upset.

Samples of air taken at various points and stages of the process showed lead concentrations ranging from 1·137 to 2,120·0 mgm. per cubic metre according to the operation involved, due to lead dust from the revolving brushes and emery wheels and to lead fumes from a filler paste which is used hot. A lead concentration of 0·15 mgm. per cubic metre of atmosphere is taken as the tolerance threshold when exposure is continuous for 8 hours daily.

Specimens from the workers exposed showed an average 89 μgm. lead per 100 cc. of blood, 26 μgm. coproporphyrin per 100 cc. of urine and 700 basophils per million cells.

Control measures, which seemed to have overcome the trouble, included a return to hand filing, extractor hoods over the hot lead paste and improved ventilation generally, continuous flushing of the working floor during each shift and vacuum sweeping between shifts. Each worker was allotted the tasks which exposed him to the hazard for only 1 month out of every 3 and was given phosphoprotein in tablet form daily and an EDTA preparation for the last week during the month at risk. A medical check-up at the end of this aimed at excluding any workers who proved particularly susceptible from further exposure. *J. Cauchi*

ROCHE, L., LEJEUNE, E., TOLOT, F., MOURIQUAND, C., BARON, GOINEAU & SOUBRIER. Saturnisme et thalassémie. **[Lead Poisoning and Thalassaemia]** *Arch. Maläd. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 329–33.

These diseases in their classical form are obviously different, but diagnosis may be difficult between minimal thalassaemia and lead absorption. The blood picture may be similar in both. The existence of hypochromic anaemia with basophil stippling and increased serum iron can, in the absence of characteristic clinical signs, be a source of confusion; target cells are found in a proportion of cases of hypochromic anaemia, whatever the aetiology.

Laboratory tests which can be used to distinguish between the diseases are enumerated, and their value shown when the possibility exists of both diseases being present. Clinical and laboratory findings in 4 patients of Mediterranean stock include splenomegaly, hypochromic anaemia with numerous abnormal cells and increases in alkaline-resistant haemoglobin, haemoglobin A2 and osmotic resistance, indicating thalassaemia. In 3 of them, urinary coproporphyrins were 92, 60 and 150 μgm. per 24 hours. Chelation with EDTA was followed by excretion of 1,000–2,000 μgm. Pb daily in 2 of these, and they had been exposed to lead in their work. The fact that stippling persisted after chelation confirmed thalassaemia, but lead absorption was also diagnosed. The sister of one of these patients was found to have thalassaemia, and so were the children of another in whom chelation was not followed by such high Pb excretion or by decrease in stippled cells; no lead risk was found in his work or in his home environment.

The question is raised whether thalassaemia renders patients more sensitive to the effects of lead than healthy subjects. Investigations are being made to see whether the basophilic granulated cells are morphologically similar in the 2 diseases.

M. Patricia Fitzsimons

ALBAHARY, C. Saturnisme et troubles de l'hémoglobinogénèse. **[Lead Poisoning and Disturbance of Haemoglobin Formation]** *Arch. Malad. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 352–6.

This discussion followed the paper on Lead Poisoning and Thalassaemia [see ROCHE *et al.*, above]. A résumé of haemoglobin disorders associated with the presence of basophil granulated cells shows that this finding does not diminish the diagnostic significance of these cells when lead poisoning is suspected. Confirmation, if doubt exists, is simply by measuring the amount of lead excreted after administration of a chelating compound. Results of several kinds of blood and urine investigations, including alkaline resistant haemoglobin and electrophoresis, are given for patients in whom stippled cells were found, and also for their relatives. One was a young Chinese dwarf with osteoporosis who was affected by C homozygote haemoglobinosis.

Stippling, evidence of an upset in the synthesis of haemoglobin, is found in minor and minimal thalassaemia and in lead absorption, and a thalassaemic subject may be exposed to lead in his work. The relative value of each blood investigation is discussed in the differential diagnosis of these and other diseases, and also the mechanisms which bring about stippling. Lead seems to act as an antienzymatic substance, either on chelation of iron or on porphyrin synthesis, whence the formation of stippled cells and the persistence of iron-containing particles which are not made use of. Uncertainties as to

the stage at which lead exerts its influence on cells do not discredit the almost specific evidence given by stippling that lead is stored in the organism.

M. Patricia Fitzsimons

SANO, S., INOUE, S., HARADA, A. & ORITA, Z. **Relation between Free Protoporphyrin and Haemoglobin in Red Blood Cells in Lead Poisoning.** *Acta Scholae Med. Univ. in Kioto.* 1960, v. 36, No. 3, 182–5, 1 fig.

Porphyrin concentrations in urine and blood from 31 lead workers are shown in relation to blood counts and to the average values from 10 healthy men. A table sets forth the results of determining urinary coproporphyrin, erythrocyte and plasma copro- and protoporphyrin, erythrocyte counts, haemoglobin, haematocrit, reticulocytes and stippled cells. Urinary coproporphyrin was increased in 19 men. Protoporphyrin concentrations in erythrocytes were greatly increased in all, 14 of whom had anaemia. Stippled cells were increased in all, especially in those with anaemia, but there was no correlation between protoporphyrin concentrations and number of stippled cells. All complained of symptoms suggestive of lead absorption.

The remarkable increase of free protoporphyrin, 10 to 50 times greater than normal values, in the men with normal blood counts suggested hypersynthesis of porphyrin apart from that for normal haem formation. Experiments to elucidate this show the effects of vitamin B12 and folic acid on rabbits intravenously injected with lead acetate in glucose solution (1 mgm. Pb) daily for 30 days. In the vitamin group (19 mgm. B12 and 15 mgm. folic acid daily) erythrocytes and haemoglobin did not decrease as they did in the untreated group. In both groups, protoporphyrin concentrations in erythocytes increased to the same degree, and coproporphyrin in the urine did not differ. Possible explanations, apart from the biosynthesis of porphyrin and haem taking a different course, are that preliminary hypersynthesis of porphyrin is followed by haemoglobin formation from this increased protoporphyrin in the presence of B12 and folic acid, or that these 2 substances play an important role in globin formation. Studies on globin formation are necessary.

M. Patricia Fitzsimons

SANO, S., TANABE, Y. & SUMIYA, C. **The Metabolism of δ-Aminolaevulinic Acid, Porphobilinogen, Uroporphyrin and Coproporphyrin in Lead Poisoning.** *Acta Scholae Med. Univ. in Kioto.* 1960, v. 36, No. 3, 186–90, 3 figs. [17 refs.]

Urinary excretion of these substances was determined in 4 experiments with rabbits. In 1 group, Pb poisoning was brought about by 5 subcutaneous injections of lead acetate solution (20 mgm. Pb per kgm.). In the second, porphyria was induced by oral administration of allyl-isopropylacetamide or Sedormid, 200 mgm. per kgm. for 10 days. A saline solution of 50 mgm. of delta-aminolaevulinic acid (δ-ALA) was injected intravenously in rabbits poisoned with Pb and normal rabbits. Methods are described for determining δ-ALA and porphobilinogen (PBG) in blood; crystalline PBG was supplied by Professor C. RIMINGTON, whose method was used.

In the first group, δ-ALA and PBG increased in the blood, notably and simultaneously after 10–13 days. High urinary levels ran parallel with increase of coproporphyrin. Excretion of δ-ALA was twice or thrice that of PBG, and maximum excretion of both coincided with maximum stippled cell counts. In the second group, much higher levels of all 4 substances were excreted, the δ-ALA being one-third to one-half of PBG.

After administration of δ-ALA, the rabbits poisoned with Pb excreted much less PBG and uroporphyrin than the normal animals, and twice as much coproporphyrin III. The significance of these findings is discussed in relation to previous work, and the pattern of porphyrin metabolism in Pb poisoning is shown in a diagram, the first disorder consisting of hypersynthesis of δ-ALA from glycine through the effect of mitochondria of erythroblasts and stippled cells. The hypothesis that the conversion of δ-ALA into PBG is inhibited seems to be favoured, and in Sedormid poisoning this conversion is accelerated. The coproporphyrinuria in Pb poisoning might be explained by coproporphyrinaemia with consequent increased excretion and by conversion of the increased blood δ-ALA and PBG into coproporphyrin by mitochondria in the kidney.

M. Patricia Fitzsimons

PETROVIC, L., STANKOVIC, M., SAVICEVIC, M. & POLETI, D. **Aerosol Inhalation of $CaNa_2$ E.D.T.A. (Mosatil) by Workers constantly exposed to Lead Poisoning.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 201–4, 2 figs.

Lead smelters were admitted to hospital in Belgrade for investigation of lead excretion after continuous or interrupted adminstration of an aerosol containing solutions of $CaNa_2$EDTA. The first group of 5 men received 0·6 gm. daily for 7 days and 2·4 gm. on the 9th day. The second group of 5 received 2·4 gm. on alternate days 4 times. They had been working in a plant where the atmospheric concentrations were 0·6–1·25 mgm. lead oxide per m^3.

In the first group, the urinary lead rose sharply to 2,500 mgm. per 24 hours, decreased as sharply when treatment was discontinued and increased to 3,500 on the 10th day. In the second group, urinary excretion fluctuated markedly each day, the peaks on treatment days becoming successively lower from nearly 3,500; low levels were found on 3 days after treatment ceased. Urinary coproporphyrin fell to normal in both groups. Individuals vary in the degree to which they absorb EDTA. The first group excreted on the average 21·6 mgm. Pb after a total dose of 6·6 gm. EDTA to each man, the second excreted 14·2 mgm. though each received 9·6 gm. Daily inhalation seemed more effective. In both groups, blood lead levels of 0·1 mgm. per 100 ml. fell by 20–45% during treatment. Stippled cell counts showed some irregularity.

M. Patricia Fitzsimons

SMITH, J. C. & WELLS, Agnes R. **A Biochemical Study of the Urinary Protein of Men exposed to Metallic Mercury.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 205–8, 1 fig. [17 refs.]

Proteinuria is not often found in chronic Hg poisoning, but protein was found in the urine of 3 men who had been exposed to Hg vapour for 2 years. Urinary concentrations per litre were 0·3 gm., 1·3 gm. and 1·6 gm. of protein and 990 μgm., 180 μgm. and 430 μgm. of Hg. Before exposure there had been no proteinuria, and removal from exposure resulted in cessation in the first 2 and reduction—in a changed form—in the 3rd, in whom, 1 year later, chronic nephritis was diagnosed. Evidence, from investigations made on the nature of the protein at the time of its discovery in the 2nd and 3rd man, lead to the conclusion that exposure to Hg resulted in the appearance of serum proteins in the urine. This was presumably caused by a kidney lesion which was reversible because of their disappearance in 1 case and, in the other, the change in the electrophoretic pattern—mainly the disappearance of the large globulin fraction and the predominance of albumin found later. At first the urinary proteins exhibited the same electrophoretic pattern in both cases, with a preponderance of globulin. The molecular weight of the mercury urinary protein was near to that of serum albumin. Urinary free amino acids were within normal limits. Amino acid analysis of the electrophoretic components showed that each was indistinguishable from those found in nephritic patients. The bound carbohydrate values were similar to those found in nephritic urinary protein. Immunological tests showed similarity of antigenic structure to serum and nephritic urinary proteins.

Clinical details are given of the case of chronic nephritis but it would be premature to connect this disease with the previous exposure of Hg.

M. Patricia Fitzsimons

JENNY, G., CHAUMONT, A. J., WEIL, E. & JENNY, G. Les risques d'hydrargyrisme dans les ateliers de fabrication de thermomètres. Résultats d'une enquête. [**Risks of Mercurialism in Thermometer Manufacture. Results of a Survey**] *Arch. Malad. Professionnelles.* Paris. 1960, July–Aug., v. 21, Nos. 7/8, 439–55, 5 figs. [42 refs.]

When mercurialism was found affecting thermometer makers employed in various concerns in eastern France, an environmental and clinical survey was made in the 4 principal thermometer factories. It shows that the disease is still too common, owing to working methods and conditions that have scarcely changed since the beginning of the century, although automatic filling has decreased the risk slightly. In the remaining processes, which are described, Hg has to be manipulated, and this explains why skilled workers may be exposed to the vapour, even in a well-appointed factory where the 2 hazardous processes, filling and sealing, were carried out in 2 separate rooms. Here, all workrooms were clean and airy, walls, ceilings and floors were smooth, no globules of Hg were visible on benches and ground and amenities were good, and yet about 20% of the workers had signs of Hg poisoning. Environmental conditions were very different in the other factories. Workers theoretically not exposed to Hg were occupied on other processes in the same room. Mid-room atmospheric concentrations of Hg in all 4 factories bore no relationship to the incidence of mercurialism. Generally they were near the maximum permissible limit of 0·1 mgm. per m^3, but values of 0·15, 0·2 and 0·35 were found.

Erythrism was present in 15 of the 36 workers; 13 had tremor; other symptoms were less frequent, but in almost every case Hg was found in the urine. Excretion was estimated by 2 quantitative methods which are described in detail, and standardization curves are illustrated. A table shows fairly close correlation between clinical and urinary findings. Less than 20 μgm. of Hg per litre can be disregarded as within non-pathogenic limits, but more, in thermometer workers, indicates that a search should be made for symptoms and 30 μgm./litre means that poisoning is more than probable.

Among preventive methods, continuous atmospheric monitoring is stressed as being necessary in some positions; if this is not possible, frequent estimations should be made. Urinary estimations should be carried out more frequently than in the past.

M. Patricia Fitzsimons

LUNDGREN, K. D. & SWENSSON, A. **A Survey of Results of Investigations on Some Organic Mercury Compounds used as Fungicides.** *Amer. Indust. Hyg. Ass. J.* 1960, Aug., v. 21, No. 4, 308–11, 4 figs. [22 refs.]

This summary of Scandinavian work includes field investigations in factories, seed dressing stations and the paper industry. Though the acute toxicity of different alkyl Hg compounds, phenyl Hg compounds and inorganic Hg salts is much the same, the effects of poisoning are different and the risk of poisoning from alkyl Hg is greater. This is partly because it is more volatile and the Hg in it is excreted more slowly than after equivalent amounts of Hg as phenyl or inorganic Hg—provided in the case of the latter that there is no kidney damage—and not, apparently, because of central nervous system fat solubility. The Hg content of the brain is less than that of the blood, and the ratio between them is lower for alkyl Hg than for phenyl Hg and seems highest for inorganic salts [this *Bulletin,* 1959, v. 34, 1266; 1960, v. 35, 348, 436].

In the field surveys high urinary Hg values were found, but clinical examination showed no signs of central nervous damage. Excretion values fell as factory conditions and equipment in stations improved, demonstrating that increased quantities of alkyl Hg compounds could be handled safely. It was not possible to tell how much Hg in the urine was due to exposure to metallic Hg and how much to alkyl Hg. In paper factories where alkyl and phenyl Hg compounds were used, atmospheric Hg was metallic vapour resulting from decomposition of the compounds, and a method was found by which metallic and organic vapours could be determined separately. If this could be done in urine, it might explain some of the contradictions in the literature.

M. Patricia Fitzsimons

MORGAN, J. G. **A Simplified Method for the Estimation of Nickel in Urine.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 209–12. [13 refs.]

An increase in the nickel content of urine within a few hours of accidental inhalation of nickel carbonyl can be demonstrated by means of a modified Sandell's test which is described. Men working on the production of carbonyl at Clydach, Swansea, are instructed to attend the medical department if they have a headache or think they have been exposed. Oxygen administration is started. Blood samples are taken immediately for estimation of nickel and CO. Later, a urine sample is taken and the nickel content is compared with that previously found at the individual's routine periodical examination. Tables show serial estimations, starting 3 days after inhalation, in 15 men who were ill and did not report immediately and who were subsequently away from work, and, starting on the 1st day, in 8 men who lost no time from work. The latter began 2 days' versenate therapy immediately, the former, 4 days' therapy on the 3rd day. Maximal values were reached about the 4th day. It took 10 to 14 days for normal values to be gradually regained. No quantitative relationship was found between urinary nickel and severity of symptoms and signs.

In persons not engaged in the nickel industry, the urine may contain 0·01–0·03 p.p.m. nickel. Among applicants for employment, the average was 0·04 p.p.m. At routine examinations, the urine contained 0·008–0·15 p.p.m. where carbonyl was produced or used, and in other processes, 0·01–0·043 at furnaces, 0·005–0·06 in chemical precipitation plants and 0·002–0·05 in calcination plants. Among the 15 men who were ill, pre-accident values ranged from 0·09 to 0·98; 4th day, 0·4 to 2; 8th day 0·2–0·9 p.p.m. Among the other 8, 1st day values ranged from 0·1 to 0·8; 2nd day, 0·2–2·9; 8th day, 0·15 to 0·9 p.p.m. *M. Patricia Fitzsimons*

SCHUCHMANN, W. Meine Thallium-Vergiftung. Eine Untersuchung der Ursachen der Giftwirkungen und des Schadens. **[My Poisoning by Thallium]** *Desinfektion u. Gesundheitswesen.* 1959, Nov. & Dec., v. 51, Nos. 11 & 12, 159–65; 175–6. [12 refs.]

In this remarkable paper the author describes his own case of poisoning by thallium which led to severe invalidism. This is preceded by an account of considerable length, of rats and their dangers to man, the destruction of rats, pesticides which contain thallium and the poisonous effects of thallium. There follows a description of the precautions which should be taken in the use of thallium and of the official regulations which govern this use.

The author, who was employed at a works where motor car brakes are repaired, gives a lengthy account of the works building, the methods of its cleaning, the provision of food and drink on the premises and their infestation by rats. Ultimately a plan to destroy rats by a thallium-containing paste (Zelio) was introduced in May 1958, and is described. This plan in many respects did not conform either with the official regulations or the recommendations of the firm which produce the Zelio paste.

At the beginning of June 1958 he began to suffer from pains in the legs which were diagnosed and treated as rheumatism. The pains continued for some weeks and he then noticed a slight falling out of his hair. In August 1958 he had a second attack of poisoning with severe nervous symptoms, abdominal colic and pains in the legs again diagnosed by two physicians as rheumatism. At length the diagnosis of thallium poisoning was made in Frankfurt. His sight became severely affected and in the eye clinic he was treated by about 500 intramuscular and intravenous injections, 120 intraocular injections and surgical operations. He gives an account of his grievous present disability which has been assessed at 70%.

In the continuation of the paper there is an account of the investigations carried out by the authorities for several months to discover how the poison came to be taken. At first there was a suspicion that the thallium had been administered in an attempt at murder but no evidence of this was forthcoming and the mystery remains unsolved. *M. E. Delafield*

ZURLO, N. & METRICO, L. **Simple Methods for Microdetermination of Industrial Toxics in Air.** *Med. d. Lavoro.* 1960, Apr., v. 51, No. 4, 241–358, 8 figs. [Numerous refs.]

The authors summarize some of the analytical methods used at the Montecatini Laboratory of Industrial Hygiene in Milan for the determination of toxic substances in industrial atmospheres. Preference is given to simple methods. Procedures that require particular equipment and specialized laboratories are omitted, so that methods for the determination of a number of metals are excluded, and other determinations that require troublesome procedures are omitted. Nevertheless procedures are given for the determination of a long list of substances. For each method there are given the essential information for a reliable analysis, with bibliographical references. Most of the methods described are liable to errors of ± 10 per cent., but for practical purposes errors of this magnitude are not of serious consequence.

The reader is warned that the methods should be accurately controlled by determinations on known quantities of the substances to be tested, and that such control should be repeated periodically on account of the instability of the reagents. In connexion with air pollution, determinations are made on very small amounts of material, so that small deterioration in reagents may cause large errors. Highly diluted solutions should be prepared immediately before tests, and samples should be analysed as soon as possible after absorption from the air.

The contaminant is removed from the air by washing the sampled air with a solution able to adsorb the contaminant to be determined. Consideration of absorbers is limited to 3 devices:—(a) the Drechsel unit or fritted glass bubbler, (b) the impinger, and (c) the glass-pellet absorber. These are illustrated and discussed.

For sampling small quantities of air, up to 5 litres, aspiration by water reflux can be obtained with the Mariotte bottle. For sampling larger volumes a water or electric pump is required.

For each toxic substance in the text a maximum allowable concentration (MAC) is indicated. The MAC is defined as the maximum concentration that can be tolerated without consequences by a healthy person exposed to the contaminant for 8 hours a day 6 days a week. The MAC is based partly on experience in industry and partly on the results of animal experiments. For some substances the tolerable limits are known with considerable accuracy. For others the MAC is calculated on the basis of such few data as are available, and these values are subject to continuous revision and adjustment in the light of experience.

For each of the methods described the volume of air to be sampled is indicated. Notes are given of possible interference due to the presence of other substances in the air.

[This publication should be of substantial value in any laboratory which is concerned with the examination of industrial atmospheres. Although it appears in an Italian journal it is printed in English.] *Thomas Bedford*

CHALUPA, B., SYNKOVÁ, J. & SĚVCÍK, M. **The Assessment of Electroencephalographic Changes and Memory Disturbances in Acute Intoxications with Industrial Poisons.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 238–41. [12 refs.]

An experimental memory examination was given to 22 patients after any disturbance of consciousness was over, and this was followed by an electroencephalogram. Carbon monoxide had been inhaled by 12, acetone, methyl chloride, methyl bromide or trichloroethylene by 5 and the last mentioned was ingested by the remaining patients. The average values of the memory tests when compared with those of healthy controls showed disturbances of logical memory and decrease of accordance in recognition, while the least injury was suffered by the mechanical memory; the reproductive tendency and the percentage of false reproductions in the recognition test were increased. An evaluation of the changed memory components was made. Since up to 2 of 5 pathognostic signs were found in the controls, patients with 2 or less signs in the test were regarded as within normal limits. The classification of results, the EEG classification and clinical sequelae are presented in a table which separates the cases into mild, moderate or severe intoxication; the last group of 6 all had loss of consciousness, and so had 5 of the 10 in the moderately intoxicated group. Memory disturbances increased with the degree of intoxication, and, although there were differences and anomalies within the groups, there was general accord between the EEG findings and the number of pathognostic signs in the memory tests. The numbers of pathological findings in the 3 groups in EEG and memory were: 0 and 2; 7 and 6; 5 and 5. The 2 examinations may be of value in assessing the degree of intoxication and sequelae from such poisons.

M. Patricia Fitzsimons

FABRE, R., TRUHAUT, R. & LAHAM, S. Recherches toxicologiques sur les solvants de remplacement du benzène. IV. Étude des xylènes. **[Toxicological Investigations on Solvents which may Replace Benzene. IV. A Study of the Xylenes]** *Arch. Malad. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 301–13, 4 charts & 3 figs. [36 refs.]

Prolonged inhalation of xylol by rabbits and rats formed this part of research on preventing benzene poisoning because, in effect, only acute xylol poisoning had been described in the literature. An account of the 3 isomers of xylene is followed by a review of the literature. The xylol used in the experiments was found to be free of benzene and toluene and consisted of about 52% *meta*-xylene, 27% *ortho*-xylene and 21% *para*-xylene. Strong concentrations, 5 mgm. per litre of air, were administered to rabbits for 40–55 days, and weaker concentrations, 3 mgm., to rabbits and rats for 110–130 days. Both groups were exposed for 8 hours daily on 6 days each week. Tables, graphs and kidney sections illustrate the results.

In both groups there was slight leucopenia and the marrow was hyperplastic; at the high concentration, there was anaemia, and increase in thrombocytes; these abnormalities disappeared more quickly and were less severe than those caused by equivalent concentrations of benzene.

Histological examination, in addition to vascular congestion, particularly of the liver, kidneys, heart, suprarenals, lungs and spleen, showed that the kidneys were affected by a subacute glomerular nephritis. This indicates the need for prudence in the use of xylenes.

Tissue distribution concentrations show that the xylenes, like benzene and toluene [this *Bulletin*, 1955, v. 30, 784], had, by 130 days, accumulated most in the suprarenals, marrow, spleen and central nervous system. This last localization tallied with disorders of equilibrium and hind-quarter paralysis observed terminally in some of the rabbits exposed to the high concentration. This group had conjunctival irritation, anorexia and marked loss of weight by 7 days, and later became drowsy with difficulty in breathing at the end.

M. Patricia Fitzsimons

FABRE, R., TRUHAUT, R. & LAHAM, S. Recherches sur le métabolisme comparé des xylènes ou diméthylbenzènes. **[Investigations Comparing the Metabolism of Xylenes or Dimethylbenzenes]** *Arch. Malad. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 314–28, 9 figs. [25 refs.]

Reproductions of infra-red spectra and of X-ray diffraction spectra show that the metabolites corresponding to the oxidation of the particular xylene isomer administered—which were excreted in the urine, were similar in 3 species of animals. Breakdown products of the 3 isomers are illustrated by structural formulae in the review of the literature and the discussion of results. Solutions of *ortho*-, *meta*- or *para*-xylene in olive oil were administered intragastrically in doses of 0·4 ml. per kgm. each day for 1 week to rats, guineapigs and rabbits. Techniques used in isolating *ortho*-, *meta*- and

para-toluic acids and the xylenols from the urine are described. Identification of these metabolites was done by means of melting points and analysis of elements as well as by comparing spectra with standards.

Each xylene was transformed, by oxidation of one of its methyl groups, into the corresponding toluic acid. Chromatography did not reveal the presence of *ortho*-, *meta*- or *tere*-phthalic acids, confirming that the second methyl group was not oxidized. With all 3 xylenes xylenols were excreted, showing that oxidation of the ring took place. With *ortho*-xylene, for the first time, the xylenol, dimethyl-3·4-phenol-1 was identified in crystalline form, and the possibility of the formation of another *ortho*-xylenol is suggested. With *meta*-xylene, chromatography showed the presence of phenolic products. With *para*-xylene, the formation of dimethyl-2·5-phenol-1 in the rabbit was confirmed and this metabolite was also found in the other animals; in addition, hydroxytoluic acids were found, but which of the 4 isomers possible was not elucidated. Further investigations on a quantitative basis will be completed.

M. Patricia Fitzsimons

Gerritsen, W. B. & Buschmann, C. H. **Phosgene Poisoning caused by the Use of Chemical Paint Removers containing Methylene Chloride in Ill-Ventilated Rooms heated by Kerosene Stoves.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 187–9.

Widely used non-inflammable chemical paint removers contain chlorinated hydrocarbons, most likely methylene chloride, as the main solvent. Case histories of 2 patients show that lethal or dangerous concentrations of phosgene can be formed within 3 hours if such removers are used in badly ventilated rooms where a kerosene stove is burning. Experiments in a closed cupboard of 6 $m.^3$ capacity in which a stove was burning resulted in lethal concentrations in 5 to 10 minutes; in the cupboard was placed a painted board treated with approximately 50 gm. of a remover which had the same composition as the one used by the deceased patient; it contained 92% volatile solvent, almost entirely methylene chloride. Samples of air, withdrawn at intervals at a height of 1·3 m. contained phosgene, *e.g.* after 11 minutes, 32 p.p.m., after 26, 68 p.p.m. after 54, 12 p.p.m., and higher concentrations were obtained with 54·3 gm. remover. In other experiments, phosgene was estimated continuously for 20 minutes with results of 750 and 760 mgm. per $m.^3$. In experiments without the stove, the concentrations of methylene chloride were 700 and 1,300 mgm. per $m.^3$. Under the severe conditions of these tests, methylene chloride was decomposed at a high rate, phosgene being the main product.

Ventilation is obviously necessary where such paint removers are used, but danger is accentuated by their description as "non-inflammable" which might imply, wrongly, that heating by combustion stoves unconnected to a chimney is permissible; even with electric fires, decomposition products may be harmful.

M. Patricia Fitzsimons

Cornish, H. H. & Block, W. D. **A Study of Carbon Tetrachloride. II. The Effect of Carbon Tetrachloride Inhalation on Serum and Tissue Enzymes.** *Arch. Environment. Health.* Chicago. 1960, Aug., v. 1, No. 2, 96–100, 3 figs. [12 refs.]

Continuing previous work [this *Bulletin*, 1960, v. 35, 1091], the authors investigated the relationship of serum and liver enzymes in rats after fasting for 1–6 days and during 9 days following a single 4-hour exposure to 6,000 p.p.m., CCl_4, a concentration which would produce maximum changes. The data on liver enzymes were calculated per gm. of liver nitrogen. Serum proteins, determined because an alteration in fluid balance could affect serum enzyme concentrations, showed minor increases in both groups.

In the fasting rats, utilization of glycogen was shown by a decrease in liver weight percentages, and liver nitrogen values increased. Liver xanthine oxidase decreased after 24 hours and liver GOT increased after 2 days. Liver esterase and the 3 serum enzymes were unaffected.

In the exposed animals, though they failed to eat for at least 24 hours, the percentage of body weight attributable to the liver increased because of rapid accumulation of liver fat, and liver nitrogen values decreased. Both returned to normal in 5 days. Figures show serial relationships of the enzymes, as percentages of control value, 100%. Esterase values after 1 and 2 days were 160% and 50% in serum, 20% and 10% in liver. Xanthine oxidase values increased rapidly in serum to 1,100%–1,200% and decreased to 40% in liver. GOT values increased 55 times in serum and to 180% in liver after 1 day. By 4–5 days after exposure all enzyme values were normal and afterwards the esterases and liver GOT were above normal. When the liver enzymes were plotted on the basis of the total enzyme content of the entire liver, the curves were essentially the same as those from liver nitrogen, indicating that the figures represent actual increases or decreases of activity.

The relationships between serum and liver enzymes reflect release from damaged tissue into the blood, rate of removal or inactivation in blood and rate of resynthesis in damaged tissue. *M. Patricia Fitzsimons*

Torkelson, T. R., Oyen, F. & Rowe, V. K. **The Toxicity of Bromochloromethane (Methylene Chlorobromide) as determined on Laboratory Animals.** *Amer. Indust. Hyg. Ass. J.* 1960, Aug., v. 21, No. 4, 275–86, 2 figs. [14 refs.]

Toxicity and 2 methods of determining blood bromide concentrations were investigated to clarify contradictory data [this *Bulletin*, 1948, v. 23, 268; 1949, v. 24, 49; 1953, v. 28, 638, 959], and 8 tables of results are given in 5 species of animals. Consequently, 400 p.p.m. for 7–8 hours' exposures, with a time-weighted average not to exceed 200 p.p.m., is suggested for bromochloromethane, an effective fire-extinguishing agent.

To determine the minimum and maximum intensities to produce respectively 100% mortality or no deaths, and the maximum to cause no pathological changes, matched groups of rats were exposed to single concentrations of CH_2BrCl ranging from 80,000 p.p.m. to 600

p.p.m. for periods of 0·1 hour to 7 hours. At high intensities prolonged anaesthesia was the cause of death, and delayed deaths in survivors were exceptional. A figure compares these results with the vapour toxicity of carbon tetrachloride and shows CH_2BrCl to be less toxic: *e.g.*, in 0·25 hour over 26,000 p.p.m. CH_2BrCl were required before it was lethal while the comparable CCl_4 concentration was over 12,000 p.p.m., and maximum concentrations which did not cause injury were 7,500 and 1,200 p.p.m. respectively.

Full pathological examinations included blood nitrogen determinations and blood counts in repeated 7-hour daily exposures on 5 days each week. No bromism was noted, though all species had elevated bromide levels. Where adverse effects were found they were limited to increases in liver weight, with only microscopic evidence of injury which was apparently reversible, and increases in kidney weights; though guineapigs showed testicular changes also, the females showed no adverse effects except leucocytosis. Rats, rabbits, guineapigs and mice exposed to 1,000 p.p.m. for 4 months showed adverse effects, but not at 500 p.p.m., except female rats. Female rats and dogs showed no effects of consequence at 370 p.p.m. for 6 months. In rabbits, instillation caused conjunctival and temporary corneal irritation; skin application caused only defatting, but covered application for 24 hours with 5 gm. per kgm. caused burns, 4 of 5 rabbits surviving this, with only slight loss of weight.

Serial blood bromide determinations were also made in rabbits repeatedly exposed, as above, to 130 p.p.m. for 2 months, and both the ashing technique (Shrader, *Indust. Eng. Chem., Anal. Ed.*, 1942, v. 14, 1) and the gold chloride method (Wuth, *J. Amer. Med. Ass.*, 1927, v. 88, 2013) were used. Results with these techniques were compared in rabbits after oral doses of NaBr, 0·5–2 gm. per kgm., with reasonable agreement provided factors were used to convert NaBr to bromide ion, and blood to serum values. All results were converted to Br^-. Blood bromide ion concentrations reached maximum, 30–35 mgm.% Br^-, in 2 weeks. After 6 months' exposure to 370 p.p.m. they were 44–73, and 4 months after 1,000 they were 122 mgm.% Br^-.

M. Patricia Fitzsimons

Hill, W. H., Kuhns, L. J., Merrill, Jean M., Palm, Betty J., Seals, J. & Urquiza, U. **Determination of Decaborane and Pentaborane by means of Triphenyltetrazolium Chloride.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 231–8, 6 figs.

This is a history, illustrated by figures and tables, of the steps in experiments to devise a quantitative test for these boranes, undertaken since the observation was made that the reagent, triphenyltetrazolium chloride (TTC) gives a red colour with decaborane and with pentaborane. An alkaline solution of TTC was reduced by decaborane to the corresponding water insoluble formazan which was soluble in many solvents such as xylene and dioxane. Xylene in a bubbler which also contained alkaline TTC became red when pentaborane in nitrogen was passed through. Some quantitative relationship was established during animal inhalation studies. Maximum spectrophotometric absorption occurred at 490 millimicrons. A single phase system—TTC, the alkali, water and organic solvent—and a 2-phase system composed of an aqueous and an organic layer were investigated. Various solvents, amines to act as organic "alkalis" and analogues and homologues of the reagent, which were tried and abandoned, are discussed. Single phase systems based on pyridine as a mutual solvent became the most commonly used; pyridine gives no blank colour with TTC and gives fine colours with boranes and TTC.

The difficulties of constructing a dependable calibration curve were overcome as a result of knowledge gained from experiments to measure the effect on the pentaborane-TCC colour reaction of time, amount of boron, strength of aqueous pyridine and the sequence of adding reactants. After similar investigations, standardization curves were constructed for a decaborane-TCC reaction—in a 2-phase system with aqueous NaOH and xylene, and in a 1-phase system of aqueous pyridine and a dispersing agent. Concentrations of TTC from 1–5% seemed best for both boranes, and the TTC reaction can be applied to diborane and probably to many derivatives of boranes. *M. Patricia Fitzsimons*

Goldstein, I. & Popovici, C. La valeur toxicologique des dérivés ferrugineux de la protoporphyrine dans l'intoxication par les nitro-amino dérivés aromatiques. **[A Toxicological Valuation of Iron-containing Derivatives of Protoporphyrin in Poisoning by Aromatic Nitro-amino Compounds]** *Arch. Malad. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 334–42, 2 figs. [15 refs.]

This work from Bucharest extends previous experiments showing that methaemoglobinaemia (MHb) does not reflect accurately the course of nitrobenzene poisoning [this *Bulletin*, 1960, v. 35, 439, 866]. Serial estimations of sulphaemoglobinaemia (SHb) and MHb from the same rats are presented in figures and tables after subcutaneous injections of 0·64 gm. per kgm. (LD50), 0·3 or 0·15 gm. per kgm. nitrobenzene. Some of the first group were treated with BAL. In this group, mortality data show that the treated animals had a greater mortality and died sooner, whether the dose of BAL was 30, 20 or 10 mgm. per kgm., and similar results were obtained in another group given 0·5 gm. nitrobenzene and 30 mgm. per kgm. BAL.

In a 24 hours' study, MHb reached maximum 12 hours after 0·64 mgm. per kgm., and then fell, but the condition of most of the animals became worse and many died shortly afterwards; SHb increased steadily all the time. Mean 12 and 24 hours' values were MHb 49% and 25%, SHb 5% and 10% approximately; in treated animals, MHb was 19% and SHb 13% after 12 hours.

In 12 days' studies: with 0·3 gm. per kgm., SHb was detected before MHb appeared and continued when the latter disappeared, and in those animals where MHb was zero, SHb was found; with 0·15 mgm. per kgm. MHb appeared and disappeared from one day to another, but SHb was constantly found.

Blood catalase activity decreased during a 4 days' study to a greater degree after LD50 than in controls.

In studying compounds which are a part of the group of iron derivatives of protoporphyrin, the authors conclude that they should be considered as a whole, SHb as well as MHb, when an assessment is being made of toxicity or of permissible concentrations of compounds such as nitrobenzene, and that determinations of catalase activity would be useful. *M. Patricia Fitzsimons*

MUNARI, Maddalena & TINAZZI, V. Aspetti della patologia da anidride ftalica. [**Aspects of the Pathology from Exposure to Phthalic Anhydride**] *Rass. Med. Indust.* Turin. 1960, Mar.–Apr., v. 29, No. 2, 107–14. [13 refs.] English summary.

A clinical survey of 20 men, aged 31–55, who had been employed on the production of phthalic anhydride for 1–6 years, follows a description of the process, oxidation of naphthalene in the presence of a vanadium salt catalyst. A table gives the frequency and severity of symptoms of conjunctival and upper respiratory tract irritation, more marked in workers unloading the condensation chamber and in packaging the product, but also present in some where the work was enclosed. There was no correlation between degree of clinical findings and length of exposure.

Most of the men complained of burning, itching and running of the eyes, tingling of the nose and throat, with sneezing and a hacking cough, and hoarseness; some also reported nose-bleeding, indigestion and weakness.

Examination showed conjunctivitis with lachrymation and reddening of the palpebral margins; hyperaemia gave a velvet appearance to the tarsal conjunctiva and fornices but there was no discharge; cornea and fundi were normal. There was congestion and hypertrophy of the nasal mucosa but no ulceration. The pharynx was congested, and so was the larynx which was covered with streaks of mucus. Nothing in particular was revealed in chest examination and X-ray appearances were normal. There was no evidence of asthma, or of allergic skin manifestations. The picture of gastritis presented by some may have been associated with shift work; there was no loss of weight. Slight hepatomegaly was observed in 2 men, and 1 had hypertension and a cardiac disorder. The urine, including deposit, was normal and so were full blood counts. The question whether some symptoms may have been caused by secondary products, maleic anhydride and naphthoquinone, remained undecided.

Methods of preventing the hazard of mucous membrane irritation follow the usual lines, and it is suggested that it would be useful to use phthalic anhydride in paste form where it is handled in the manufacture of synthetic resins. *M. Patricia Fitzsimons*

BONDY, H. F., FIELD, E. J., WORDEN, A. N. & HUGHES, J. P. W. **A Study on the Acute Toxicity of the Tri-Aryl Phosphates used as Plasticizers.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 190–200. [24 refs.]

Numerous investigations in a search for a non-toxic phosphate plasticizer throw new light on the complicated story of the toxicity of the aryl phosphate esters. Reports of paralysis in man and the domestic fowl are reviewed [this *Bulletin,* 1957, v. 32, 874; 1960, v. 35, 241]. Commercial raw material used in the production of tri-tolyl phosphate (TTP) [formerly known as tricresyl phosphate] and tri-xylenyl (tri-dimethylphenyl) phosphate (TXP) was purified; phenols were isolated and the toxicity of their phosphate esters tested, generally by 5 oral doses of 500 mgm. per kgm. in chickens. Unless trained to accept a diet containing an aryl phosphate, the birds were at least 100 days old. Diagnosis was made by clinical observation, cholinesterase estimations and pathological and histological examinations. Tables show the composition of phenolic fractions used to make phosphate esters and the physical constants and toxicity of symmetrical and unsymmetrical tri-aryl phosphates.

Though the toxicity of commercial TTP is known to be due to the presence of phosphate esters containing the *ortho*-tolyl (*ortho*-methylphenyl) group, the resulting TTP was still toxic after all *ortho*-cresol was removed from the starting phenolic materials. TTP made from phenols, from which this and all *ortho*-ethylphenol was removed, was non-toxic. In the preparation of TXP, however, removal of these groups did not result in a non-toxic form.

Removal of all *ortho*-cresol, *ortho*-ethylphenol and *ortho*-propylphenol from a mixed xylenol fraction gave a phenolic mixture from which a non-toxic phosphate ester (NTP) was prepared. This was fed to a variety of mammals and to chickens in short-term tests without toxic effects; in chickens the doses ranged from 1,000 to 25,000 mgm. per kgm. Long-term feeding experiments are in progress; chickens on large doses, 5,000 p.p.m. in the diet, have not thrived as well as controls and show some central nervous system changes. The mixture from which NTP was made contained 10% of *para*-ethylphenol, and the highly toxic tri-*para*-ethylphenyl ester is present only in minute quantities. Esters containing 1 or 2 *para*-ethylphenyl groups and tri-*meta*-ethylprenyl phosphate were non-toxic. Surprisingly, an ester with a methyl group in the *ortho,* and an ethyl group in the *para* position was non-toxic.

M. Patricia Fitzsimons

HARASHIMA, S., TOYAMA, T. & SAKURAI, T. **Serum Cholesterol Level of Viscose Rayon Workers.** *Keio J. of Med.* Tokyo. 1960, June, v. 9, No. 2, 81–90, 3 figs. [15 refs.]

These investigations were made in 3 groups, aged 19–40, from 4 factories in a rural district of Japan. Social class and dietary habits were similar in all 3. Group A consisted of 64 men working in 2 artificial silk and staple fibre factories where the average CS_2 concentration was 5–19 p.p.m. and Group B of 70 in 2 staple fibre factories, concentration 15–65 p.p.m. The controls, Group C, were 48 men from clerical departments in the factories; no significant differences in cholesterol values were found within this group.

Average values of serum total cholesterol and cholesterol ester, in mgm. %, and of the ratio of esterified to total cholesterol were: Group A, 157·5, 95, 60·4%;

Group B, 212·6, 111·4, 52·8%; Group C, 154, 96·1, 62·2%. Figures show the scatter in all groups. In Group B, 7 had total cholesterol values of more than 250 mgm.%; some complained of headache, fatigue, irritability, anorexia, insomnia and pain in the legs; 5–40 micrograms CS_2 were excreted hourly in the urine, the values in Group A being 2–20.

Animal experiments, published elsewhere, showed similar results. Rabbits were exposed to 150–180 p.p.m. CS_2 for 3 hours daily on 6 days a week for 200 days. Serial estimations in a table show elevation of total serum cholesterol and decrease of ester ratio becoming more pronounced from 10 days onwards. In 2 animals, removed from exposure after 90 days, high cholesterol values were maintained for 60 days. Slight loss of weight and secondary anaemia were noted.

Serum cholesterol tests are concluded to be worthwhile in routine examinations of workers exposed to CS_2 in evaluating the intensity of exposure; a change in value may represent early chronic CS_2 poisoning if certain other diseases are excluded.

M. Patricia Fitzsimons

POWELL, M. & LOMAX, M. A. **The Toxic Effects of Handling and Firing Explosives in Coal Mines.** *Ann. Occup. Health.* London. 1960, July, v. 2, No. 2, 141–51. [11 refs.]

In the course of studies of environmental conditions made as part of an investigation of attendance among coal-miners, many men complained of headaches and other symptoms associated with the handling and firing of explosives. This report describes a brief pilot investigation which was made.

The observations were made at 15 collieries in one of the Divisions of the National Coal Board in Great Britain. 21 magazine attendants and 94 deputies and shotfirers were interviewed. General questions were also put to 450 colliers on 30 coal faces. The explosives used included nitroglycerine and ethylene glycol dinitrate, nitro cotton/cellulose, mono, di and trinitrotoluene and ammonium nitrate. These were in the form of sheathed powders and plastics, " equivalent to sheathed " powders and plastics, and unsheathed plastics. The main products of the explosion are carbon monoxide and nitrous fumes, *i.e.* nitrogen peroxide and monoxide. 54 of the 94 deputies and shotfirers alleged that they were adversely affected by handling the explosives and by the fumes. The effects included headaches, sore throat, " burning feelings " in the chest and skin rashes. Absorption occurred by ingestion, inhalation and through the skin. Shotfirers appeared to absorb nitroglycerine chiefly through the skin, particularly the skin of the forehead when wiping perspiration.

The findings are regarded as tentative but it has already been possible to suggest means whereby the toxic effects may be avoided or at least minimized.

[The toxic effects of nitro compounds used as explosives have long been known in the chemical industry. It is surprising that they are only now being discovered in coal-miners. One of the main functions of medical services in industry is to anticipate such potential hazards.] *A. Meiklejohn*

LACY, W. J. **A Comparison of the Composition of Reactor Waste Solutions and Radioactive Fallout.** *Amer. Indust. Hyg. Ass. J.* 1960, Aug., v. 21, No. 4, 334–9, 1 fig. [10 refs.]

The major biological hazards in the reactor waste after a 30-year accumulation period and a 5-year decay following accumulation are the fission products ^{90}Sr, ^{137}Cs, ^{144}Ce, ^{144}Pr and ^{147}Pm. All of these are also formed in a nuclear detonation; they are the most hazardous of the long half-life products.

The methods of dealing with these unwanted products are not the same because of a very different carrier material in the two cases. It is a complicated problem, but the essentials of the processes are succinctly described in this authoritative article. Reference is made to the recommendations of the National Committee on Radiation Protection in which may be found *Maximum Permissible Body Burdens and Maximum Permissible Concentration of Radionuclides in Air and in Water for Occupational Exposure* (N.B.S. Handbook 69, June, 1959). *S. Russ*

PARMEGGIANI, L. Contributo alla discussione dei criteri di non idoneità al lavoro che espone professionalmente alle radiazioni ionizzanti. [**Discussion on the Criteria of Unfitness to Occupational Exposure to Ionising Radiations**] *Med. d. Lavoro.* 1960, June–July, v. 51, Nos. 6/7, 442–73, 1 fig. [Numerous refs.] English summary.

See also p. 35, BALABANOFF, [**Occupational Trichophytosis of the Palms and Nails caused by *Trychophyton rubrum***]

HEATING, LIGHTING AND VENTILATION

LIDWELL, O. M. **The Evaluation of Ventilation.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 297–305, 2 figs.

The rate at which a room is ventilated is frequently measured by liberating some tracer substance and then observing the rate at which the substance disappears from the air of the room. It is assumed that the air of the room is continually and completely mixed with the incoming ventilating air, and that assumption is more or less valid in a large proportion of instances.

When the mixing of air is only partial the concentration of the tracer substance will vary from place to place within the room, and the simplest quantity that can then be used to describe the ventilation relationship between two points is the integrated concentration of tracer substance found at one point following the liberation of unit quantity of the substance at the other. The author designates this quantity the "transfer index". The reciprocal of this index is the "equivalent ventilation", and this latter approaches numerically to the rate of supply of ventilating air as the mixing of the air approaches completeness.

Nitrous oxide is a convenient tracer gas for making these measurements, and a method is also described in which acetone vapour can be used. *Thomas Bedford*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

MURDOCK, C. R., CROSSLEY, E. L., ROBB, J., SMITH, Muriel E. & HOBBS, Betty C. **The Pasteurization of Liquid Whole Egg.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Aug., v. 19, 134–52. [38 refs.]

It is recommended that liquid whole egg should be pasteurized at temperatures of not less than 147°F. (63·9°C.) for 2½ minutes to eliminate salmonellae. These recommendations are based on information summarized below; it is recognized that they are not final.

Evidence is given for the persistent contamination with organisms of the salmonella group of shell eggs (hens) and of broken-out hen egg products, prepared at home and abroad, and the danger of direct human infection and of cross contamination to other uncooked or lightly cooked foods is reviewed.

Results of experiments show the practicability of high-temperature short-time (HTST) pasteurization of liquid whole egg and its efficiency in eliminating salmonellae with the exception of some strains of Salm. Senftenberg; recommendations are given for the provision of equipment giving greater accuracy and safety.

The results of bacteriological examination including plate and coliform counts and salmonella counts, where possible, of whole egg before and after pasteurization are given for 5 plants used regularly in Denmark, England, Germany and Northern Ireland.

Baking tests with sponge and Madeira cakes, and whole egg, before and after pasteurization from the same plants, showed that there was little difference between those made with heated and unheated egg. Comparative results show the volume of foam, and volume, grain, colour and crumb consistency of the baked products.

Pasteurization is regarded as the only means by which liquid egg can be made safe for use in food establishments. *Betty C. Hobbs*

McCALLUM, May F. **Bacteriological Tests on Glasgow Consumer Milk.** *Scottish Med. J.* Glasgow. 1960, Aug., v. 5, No. 8, 350–54. [15 refs.]

From 1956 to 1959 a survey was carried out of the flora of Glasgow pasteurized and certified milk as it reached the consumer. Tests included the plate count at 37°C., and in 1958–1959 a psychrophile count at 10–15°C. and the resazurin test were compared with the presumptive coliform test.

The presumptive coliform test was favoured, the plate count regarded as cumbersome, and the resazurin test stated to be unreliable. Methylene blue was mentioned as a preferable alternative to resazurin but no comparative tests were included, nor were the Milk Special Designations for England and Wales considered. Coagulase-positive staphylococci were isolated from 26 of 40 "certified" milk samples, all strains were phage type 42D or related types, and 13 were penicillin resistant.

The standard of consumer milk was not regarded as good; poor cooling facilities and imperfectly cleaned bottles were considered to be partly responsible.

Betty C. Hobbs

SAKAGUCHI, G., SAKAGUCHI, S., KAWABATA, T., NAKAMURA, Y., AKANO, T. & SHIROMIZU, K. **Influence of Oxytetracycline upon the Toxin Production of Type E *Cl. botulinum*.** *Japanese J. Med. Sci. & Biol.* 1960, Apr., v. 13, Nos. 1/2, 13–22, 1 fig. [10 refs.]

Oxytetracycline Biostat GP was added to brain heart infusion medium, homogenized fish muscle and fish muscle inoculated directly with *Cl. botulinum* type E (strain Tenno).

With brain heart infusion broth, toxin production was inhibited by 0·2 p.p.m. oxytetracycline at 30°C., and was lessened by 0·1 or 0·5 p.p.m. The effect was enhanced by an acid *p*H, when toxin was more readily produced. The addition of 1% NaCl at *p*H 6·0 increased the antibacterial effect.

Inhibition of type E toxin production was also observed in homogenized muscle with added oxytetracycline, but decomposition of toxic activity was also rapid owing to the proteolytic activity of putrefactive micro-organisms.

Dipping fish in oxytetracycline lessened the amount of toxin produced by type E spores inoculated into the muscle. 10 p.p.m. oxytetracycline for 10 minutes stopped germination of the spores, but cold storage was essential. *Betty C. Hobbs*

FOOD POISONING

PODESTÁ, J. J., FONSECA, R., BLASCO, A. & RONCORONI, A. J. Asistencia respiratoria en el botulismo. **[Respiration in Botulism]** *Rev. Asoc. Med. Argentina.* 1960, Aug., v. 74, No. 8, 459–67, 8 figs. 3 charts. [15 refs.]

This article describes the treatment of 3 patients suffering from botulism with respiratory insufficiency. In the first, a patient aged 69, tracheotomy was performed and ventilation carried on by an Engström respirator: the patient developed pulmonary infection and died. The second patient, a pregnant woman aged 27, underwent tracheotomy and respiration was carried on by a Bang respirator: respiration was embarrassed by pressure of the uterus and a Caesarean section was performed, respiration being maintained by an Engström respirator. A normal full-time infant was delivered and the mother's respiration was greatly improved and she recovered. In the third patient respiration was embarrassed but the patient recovered without artificial aid.

The authors feel that all cases of botulism should be treated in a centre fully equipped to deal with respiratory insufficiency. *A. B. Christie*

YAMAGATA, H., IWAFUNE, Y. & SHIMAMURA, Y. **Detection of *Clostridium welchii* (Hobbs Type 6) from an Outbreak of Collective Food Poisoning.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 365–8.

This is an account of an outbreak of food poisoning which occurred among the 46 guests at a wedding party, of whom 11 were taken ill with severe abdominal pain and diarrhoea 11–14 hours after the feast. All the patients recovered after about 24 hours. A number of dishes had been prepared for the occasion by 7 neighbouring housewives and had been left in a room at a temperature of 30°C. and a relative humidity of 80% for about 10 hours before they were eaten. Some of these dishes, 6 in number—red beans with rice, broiled mackerel, soup containing mackerel fillets, chicken, octopus and raw fish—were left over and examined bacteriologically. From each of the 2 mackerel dishes a strain of *Clostridium welchii* was isolated, and no other pathogen was found. These 2 strains, designated Isami strain No. 1 and No. 2 were found on full bacteriological examination to be identical with *Cl. welchii* Hobbs type 6. Examinations of faecal material from 3 of the patients and the 7 housewives were negative. The way in which the mackerel became contaminated was not discovered.

This is the first outbreak due to this type of *Cl. welchii* which so far as the authors have been able to ascertain has been reported in the Far East, including Japan. *M. E. Delafield*

REITLER, R., YAROM, D. & SELIGMANN, Rachel. **The Enhancing Effect of Staphylococcal Enterotoxin on *Salmonella* Infection.** *Med. Officer.* 1960, Sept. 16, v. 104, No. 12, 181.

5 members of a family living in Galilee were taken ill with vomiting, diarrhoea, abdominal pain and fever, 8–12 hours after eating goats' milk cheese made by a local farmer. Chloramphenicol was given and the illness was mild. Salm. Zanzibar was isolated from all stools and from the cheese (1,000 million per gm.); no coagulase-positive staphylococci were found. 6 days later 6 members of a second family, unrelated, but living in the same district, were taken ill with more severe gastro-enteritis 3–4 hours after eating goats' milk cheese from the same batch prepared on the same farm. Chloramphenicol was given but the illness lasted 7–12 days. Salm. Zanzibar was isolated from 3 stools examined and from the cheese (1,500 per gm. only); coagulase-positive staphylococci (28 million per gm.) were also found.

It was concluded that the combination of staphylococcal enterotoxin and salmonellae caused a more severe disease than the salmonellae alone, even though the dose of Salm. Zanzibar in the first outbreak was far higher than in the second. *Betty C. Hobbs*

SEMPLE, A. B., PARRY, W. H. & PHILLIPS, D. E. **Acute Copper Poisoning. An Outbreak traced to Contaminated Water from a Corroded Geyser.** *Lancet.* 1960, Sept. 24, 700–701.

Within 5 to 10 minutes of drinking tea in a factory canteen in Liverpool, 18 out of a total of 150 employees were taken ill with abdominal pain, vomiting, diarrhoea and dizziness. All the workers affected had had tea from the same teapot. In the canteen tea was prepared in large aluminium teapots, each holding enough tea for 18 persons, with boiling water from a gas-heated geyser. No tea was left over for examination but water drawn from the geyser had a brownish tinge and sediment. Analysis of the water showed it to have a reaction of *p*H 6·7 and an amount of copper in suspension of 44 p.p.m. Examination of the geyser revealed a heavy deposit of copper sulphate in the upper and inner cover of the boiler. There was also a bare patch with no deposit and it is considered to be likely that copper sulphate from this area had been dislodged and had by chance entered the particular teapot which contained the poisonous tea. 2 of the affected workers were so collapsed that they were admitted to hospital for 24 to 36 hours. Chemical examination of their faeces showed an initial concentration of copper of 80 and 50 p.p.m. which gradually decreased during the next 4 weeks.

The geyser is of a common type, and it had been in constant use since 1949; it had never been dismantled for cleaning or scaling. It is recommended that the maker's maintenance instruction booklet should be revised.

[See also this *Bulletin*, 1959, v. 34, 262.]

M. E. Delafield

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

GRIN, E. I., OZEGOVIC, L. & ŠENFELD, M. *T. ferrugineum* u NR Makedoniji. [***T. ferrugineum* in the People's Republic of Macedonia**] Reprinted from *Nauč. Društvo nr Bosne i Hercegovine.* Sarajevo. 1960, v. 15, 11–16, 7 figs. on 3 pls., & 1 map. [23 refs.]

The English summary appended to the paper is as follows:—

"Dermatophytes of some parts of the People's Republic of Macedonia are herein described. It differs essentially in its composition from flora of other neighbouring Republics by endemic foci of T. ferrugineum. Out of 401 positively isolated cases it was found that T. ferrugineum was represented by 30.2%, T. violaceum was isolated in 59.4%, T. schoenleini and 8.5% cases, T. tonsurans 1.3%, M. audouini 0.4% and T. verrucosum 0.2% of all isolated cases.

"There are two regions on Yugoslav territory in which microsporia appears in endemic forms, in North in Serbia and Vojvodina (M. audouini) and in the South in Macedonia (T. ferrugineum). Both agents remain generally limited to their endemic foci as regionary characteristics of the spectrum of dermatophytes. Even if sporadic cases of microsporia with T. ferrugineum or M. audouini appear outside their endemic regions, they remain as a rule isolated and without tendency of infection being expanded.

"It appears that the focus of T. ferrugineum is autochthonous in Macedonia. It is not likely that the infection was brought from the Far East (Korea) or else from Africa. It is possible however that T. ferrugineum was brought into Macedonia simultaneously with the other countries of the Balkan Peninsula (Bulgaria, Albania) during the same historical epoch which is difficult to determine now."

BALABANOFF, V. A. Berufliche Trichophytie der Handteller und Nägel durch *Trichophyton rubrum.* [**Occupational Trichophytosis of the Palms and Nails caused by *Trichophyton rubrum***] *Berufsdermatosen.* Aulendorf. 1960, Aug., v. 8, No. 4, 201–14, 11 figs. (4 coloured). [19 refs.]

In this paper the author draws attention to the wide distribution of skin infections by *Trichophyton rubrum* which has become manifest since the discovery of the fungus 50 years ago by CASTELLANI and BANG. The infection may occur in children as well as adults and its clinical picture may take a number of different forms which are here classified and described with some illustrations.

In the period 1948–1959 159 patients with this mycosis were observed in the Skin Clinic of Sofia. Among these were 38 patients in whom there was a hyperkeratosis

and squamous affection of the palms of the hands, sometimes with infection of the finger nails. It is considered that in these patients the condition was of occupational origin and that there was in most instances a pre-existing infection of the soles of the feet whence it had spread to the hands which had a low resistance owing to the stresses and circumstances of occupation. In 20 patients the condition was in the right hand, in 9 in the left hand and in 9 in both hands. There is a long list of the occupations of these patients, who included housewives, locksmiths, carpenters, weavers, a gynaecologist, a gardener, a musician and others. There are 3 case histories.

There is a description with some photographs and drawings of *Trichophyton rubrum* and observations on its clinical importance and mycological relationships.

M. E. Delafield

Bouvy, L. E. & Pattyn, S. R. Traitement des teignes du cuir chevelu à l'aide de la griséofulvine. [**Treatment of Tinea of the Hairy Skin with Griseofulvin**] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 289–92.

The English summary appended to the paper is as follows:—

"Treatment by Griseofulvin of 26 cases of Tinea of the hairy skin in children at Elizabethville was completely successful in 25. Cure occurred regularly in 4 weeks. The drug was very well tolerated in all cases. With certain simple measures associated with this treatment, eviction [separation from school] is no more necessary."

Bruaux, P. Traitement de quelques cas de teignes du cuir chevelu par griséofulvine. [**Treatment of Tinea of the Hairy Skin with Griseofulvin**] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 309–25.

The English summary appended to the paper is as follows:—

"13 children affected by Tineas, 10 of whom were negroes and 3 white, were treated by daily doses of 500–750 mgm. griseofulvin. Only 7 could be followed up for a sufficiently long time to enable conclusions to be drawn; 6 of them could be considered as cured (5 microsporons, and 1 trichophyton) while in spite of treatment for 42 days, the 7th though admittedly not seen regularly, seemed to be resistant to this treatment. No toxic effects of treatment were found. In another connection the author examined the proteinograms of 10 African and one white child. In the 10 African children there was a reduction in albumin and an increase in γ-globulin (except case 12 where the latter was normal). In addition in 1 African child there was an increase in α-2 (case 5) and in another (case 4) increased β-globulins. In the European child the proteinogram was almost normal with slightly lowered γ-globulin."

González-Ochoa, A. Histoplasmosis primaria pulmonar aguda en la Republica Mexicana. Estudio de 74 casos. [**Study of 74 Cases of Acute Primary Pulmonary Histoplasmosis in Mexico**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1959, Dec., v. 19, No. 4, 341–50, 1 fig.

The English summary appended to the paper is as follows:—

"Nine epidemics and two isolated cases of primary acute pulmonary histoplasmosis are reported, discussing clinical aspects and diagnostic procedures.

"Special emphasis is placed upon the peculiarities of this form of histoplasmosis in Mexico, which are: severity of the infection reaching a lethal figure of 28·4%; constant association with bat dung; a large geographical distribution of the infection's sources, corresponding to eleven States placed in diverse regions and latitudes of the Country."

Taylor, R. L. & Dobrovolny, C. G. **The Distribution of Histoplasmin Sensitivity in Guatemala.** *Amer. J. Trop. Med. & Hyg.* 1960, Sept., v. 9, No. 5, 518–22, 3 figs.

Harland, W. A. **Cryptococcosis: a Report of Five Cases.** *Canadian Med. Ass. J.* 1960, Sept. 10, v. 83, No. 11, 580–84, 7 figs. [11 refs.]

"Five patients with cryptococcosis seen during a five-year period have been described. Two had Hodgkin's disease and one had polycythaemia vera. The fourth was malnourished and the fifth had chronic renal failure. Two had diabetes mellitus. Four of the patients had disseminated infection, including characteristic meningo-encephalitis. Certain clinical and pathological features of this disease are illustrated."

Emmons, C. W. **Prevalence of *Cryptococcus neoformans* in Pigeon Habitats.** *Pub. Health Rep.* Wash. 1960, Apr., v. 75, No. 4, 362–4.

The author of this article who was the first to draw attention to the association of *Cryptococcus neoformans* with pigeon dung in the United States [this *Bulletin*, 1956, v. 31, 523], records the results of further investigations into this problem which he carried out in or near Washington.

Samples of pigeon dung or soil contaminated by it were collected in glass tubes from various sites in various localities frequented by pigeons. Some of the material was planted on agar slants and incubated at 37°C., and some was injected intraperitoneally into mice in suspensions in order to isolate *Histoplasma capsulatum* which might possibly be present in the sample.

Results showed that 63 samples out of 91 contained *C. neoformans*.

The author is of the opinion that, owing to the existence of serological cross-reactions between cryptococcosis and histoplasmosis, there is a risk that many reactions which appear to be positive for histoplasmosis

are in fact indicative of cryptococcosis. He also draws attention to the public health hazard presented by the incidence of this organism in pigeons' dung.

[See also this *Bulletin,* 1958, v. 33, 74; 1959, v. 34, 764.] *C. J. La Touche*

DOLAN, T. F., Jr., MCCULLOUGH, N. B. & GIBSON, L. E. **Nocardiosis. Report of two Cases in Children.** *J. Dis. Children.* Chicago. 1960, Feb., v. 99, No. 2, 234–7. [19 refs.]

The first of two cases of nocardiosis in children reported in this article was that of a white boy aged 9 months who had been suffering from furunculosis since he was 2 weeks old.

In the course of clinical investigations X-ray revealed "an infiltrate in the left upper lobe and scattered nodular densities throughout both lung fields." Laboratory examination of sputum showed "finely branching Gram-positive mycelia that were weakly acid-fast," and *Nocardia asteroides* was grown when this was cultured.

Treatment included sulphadiazine and penicillin, as a result of which the lung fields gradually cleared and *N. asteroides* could no longer be recovered in culture.

Case 2 was of a white boy aged 15 years who had enjoyed good health until 9 months before admission. At this time he developed "a swelling over the medial aspect of the right knee associated with a temperature of 103°F." Operation on this site revealed necrosis of soft tissues and destruction of the periosteum of the femur. *Nocardia asteroides* was grown from material obtained at this operation. Subsequently, a swelling developed in the right calf from which *N. asteroides* was also recovered in culture.

Of possible significance in connexion with the foregoing lesions was the fact, revealed in the past history, that the patient had suffered from a chronically infected right toe. This lesion had since resolved.

Treatment again included administration of sulphadiazine and penicillin, as well as débridement of sinus tracts which had developed at the operation sites, and immobilization of the affected leg.

After the second week of treatment cultures were repeatedly negative; and 16 months later the patient had regained normal health. *C. J. La Touche*

SCHARYJ, M., LEVENE, N. & GORDON, H. **Primary Pulmonary Infection with *Monosporium apiospermum*. Report of a case with Clinical, Pathologic and Mycologic Data.** *J. Infect. Dis.* 1960, Mar.–Apr., v. 106, No. 2, 141–8, 6 figs.

The authors record and describe what appears to be one of the first detailed cases of primary pulmonary infection due to *Monosporium apiospermum* [but see also *Trop. Dis. Bull.*, 1959, v. 56, 482].

The patient concerned was a woman aged 26 years who was married to a farmer and lived in Kentucky. She was admitted to hospital on account of cough and haemoptysis on March 11th 1959. These symptoms had started a year previously. Tests did not reveal any known infective process. X-rays of the chest taken during the early part of 1959 revealed a "cavity, about 2·5 cm. in diameter in the second interspace . . . in the anterior segment of the right upper lobe" as well as other abnormal features of secondary importance.

"A diagnosis of lung abscess, of unknown etiology was made and a right upper lobectomy was performed (by N.L.) March 13." When the abscess cavity was then explored it was found that it contained "yellow granules resembling the 'sulfur granules' of actinomycosis."

Consequent on this operation, the patient made an uneventful recovery.

The authors describe in detail the gross and microscopic pathology of the resected specimen. Notable gross features observed were first of all the cavity itself which measured 3 cm. in diameter; then, the yellowish granules contained within it which measured from 1 to 4 mm. or less in diameter, and lastly a peribronchial lymph node which contained confluent foci. The microscopic features which were observed, included granulation tissue in the wall of the cavity. This included giant cells but no fungi. Fungus growth was confined to the granules which were "large" or "small." The large granules (1–4 mm. in diameter) consisted of alternate zones of "long, thin, scantily segmented hyphae and short, broad, abundantly segmented ones." The "small" granules (less than 1 mm. in diameter) consisted of an eosinophilic peripheral portion composed of "short, thick, rectangular or more nearly club-shaped elements", while the central portion was made up of "irregularly spherical or polyhedral, large, thick walled, faintly staining chlamydospores."

The cultural features of the fungus which was grown from the granules agreed with those previously described for *M. apiospermum.* *C. J. La Touche*

NEAME, P. & RAYNER, D. **Mucormycosis. A Report on Twenty-Two Cases.** *Arch. Pathology.* 1960, Aug., v. 70, No. 2, 261–8, 5 figs. [18 refs.]

Mucormycosis has, in the past, been regarded as a rare though serious mycotic complication of underlying chronic debilitating diseases, and has been most frequently associated with uncontrolled diabetes. It is therefore somewhat disturbing to read in one single report (from Durban, South Africa) of 22 cases of this disease, and still more disturbing to note that 16 of these were recorded during the first half of the year 1959.

In most of these cases some part of the digestive system was singled out by the mould concerned for the manifestations of its parasitic activity. In only 2 was the brain involved. Several systemic diseases were represented in the clinical background of these case reports, among which the most frequently mentioned are: amoebic colitis and kwashiorkor, while, contrary to expectation, diabetes is not mentioned at all. The duration of the clinical course, which terminated fatally in all cases, ranged from 2 to 70 days.

The age of the affected patients did not appear to be significant since this ranged from 3 weeks to 52 years. Likewise, the incidence did not appear to be influenced by sex since 12 of the patients were male and 10 were female.

In the digestive tract the chief histological finding was

thrombosis of the blood vessels in the affected tissues. This was also the case in other sites attacked by the moulds concerned. Previous reports of mucormycosis have also stressed this feature.

Material obtained for culture from necropsies yielded growth of mucoraceous fungi in 6 cases. This was represented by 3 species distributed as follows: 3 cases yielded *Rhizopus microsporus*, 2 yielded *R. stolonifer* (syn. *R. nigricans*) and 1 yielded both *R. microsporus* and *R. stolonifer* as well as *Mucor hiemalis*.

C. J. La Touche

WATSON, K. C. & NEAME, P. B. ***In vitro* Activity of Amphotericin B on Strains of Mucoraceae Pathogenic to Man.** *J. Lab. & Clin. Med.* 1960, Aug., v. 56, No. 2, 251–7, 3 figs.

In view of the steadily increasing number of reports on mucormycosis in man in recent literature, and in view of their own experience in connexion with this mycosis [see this *Bulletin*, 1960, v. 35, 125, 875] the authors (in Durban, South Africa) undertook a series of *in vitro* tests to ascertain to what degree amphotericin B was active against strains of the Mucoraceae.

0·5 ml. amounts of spore suspension were added to 2·5 ml. amounts of serial 2-fold dilutions of amphotericin B in sterile tubes. These were then incubated at room temperature and replicates were incubated at 37°C. After varying periods of time 0·1 ml. was plated out onto the surface of plates containing Sabouraud's agar which incorporated some bread and these were kept at room temperature for 7 days. All spores grew after being exposed to varying concentrations of amphotericin B for periods from 24 hours to 7 days. Some strains reacted to this treatment by exhibiting modifications in their morphology.

Each of 4 strains of *Rhizopus stolonifer* was inhibited at a concentration of 0·03 to 0·06 mgm. per ml. 2 of the 4 strains of *R. microsporus* were inhibited by concentrations of 0·1 mgm. to 5·0 mgm. per ml., and the strain of *Mucor hiemalis* was inhibited at a concentration of 2·5 mgm. per ml.

All strains were tested against mystatin as well and it was found that concentrations lying between 25 and 1,000 units per ml. of this drug did not inhibit any of the strains.

C. J. La Touche

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

EVANS, P. A. S. **Tuberculosis in Rural Metabeleland.** *Central African J. of Med.* 1960, June, v. 6, No. 6, 265–6.

The author refers to the increasing number of Africans found to have pulmonary tuberculosis in Matabeleland, where communications are primitive and where the difficulties of bringing tuberculous patients to hospital are very great. The disease is often acute, and to get to hospital the patient must be ill enough to decide to leave his home yet not too ill to make the long journey on foot or by bicycle, and he must be educated enough to bypass his witch doctor. The author remarks that the spirit world is very real to the African, and he shows that some of the ceremonies prescribed by witch doctors to cast out the spirits—in one instance dancing continuously for 12 hours—are dangerous. Finally there is the difficulty of ensuring that the patient will complete an adequate course of treatment, especially as most patients are men and tend to abscond when the rains start and ploughing and planting must be done. Attempts have been made to deal with this tendency, but it is difficult.

"We must appreciate these factors if we are to do our work properly, as 'we do not treat disease—we treat *people* who are sick'."

Charles Wilcocks

PROUDFOOT, L. **Tuberculosis Survey in Manus District.** *Papua & New Guinea Med. J.* Port Moresby. 1960, Apr., v. 4, No. 1, 32–3.

In a survey of this district of the Admiralty Islands 10,849 persons were tested intradermally with 1 in 1,000 OT, and the rate of positive results varied from 2·3% at age 0–1, to 35·1% at 7–14, 86·2% at 15–30, and 98% at 31 and over. The sharp rise at 15–30 is more evident in men than women, and this is associated with the fact that men of this group were in contact with the Japanese during the war; they also tend to leave home to seek work, and thus are brought into contact with the outside world. It is evident that tuberculosis is common.

The survey was a prelude to a BCG campaign.

Charles Wilcocks

KENDIG, E. L., Jr. **Prognosis of Infants born of Tuberculous Mothers.** *Pediatrics.* Springfield, Ill. 1960, July, v. 26, No. 1, 97–100.

This report is an attempt to determine the prognosis of infants born of tuberculous mothers and is a continuation of that reviewed in this *Bulletin*, 1958, v. 33, 833. The mothers had active pulmonary tuberculosis at the time of delivery, or had recent active pulmonary tuberculosis, or contracted pulmonary tuberculosis while the child was in early infancy.

Of the 83 infants, 12 received BCG; 34 of the remaining 71 infants were found to be infected with tuberculosis, and 4 of these developed tuberculous meningitis, death resulting in 3. 2 other infants died, one probably and one certainly of non-tuberculous disease. Of the 34 infected infants 20 had primary pulmonary tuberculosis demonstrable by radiography. 2 developed tuberculous pneumonia; one of these whose mother had proven miliary tuberculosis was inadvertently put to the breast once during the first 24 hours of life, and became infected at the age of 23 days, but recovered uneventfully on therapy with isoniazid and streptomycin. Of the 3 infants who had no contact with their mothers 2 died of non-tuberculous disease, the other was still tuberculin negative. The other 68 infants had minimal contact at least with their mothers, and 34 of them became infected with tuberculosis. It was noteworthy that in only 11 of these cases was the mother found to be discharging tubercle bacilli in the sputum.

Of the group of 35 infants not infected with tuberculosis, 8 were separated from their mothers at birth for periods ranging from 3 months to 2 years, and 1 has had no contact with his mother. The other 26 were in constant contact with their mothers, 14 of the mothers being considered non-infectious at the time; 2 other infants escaped infection in spite of intimate exposure to their mothers who were found to have active pulmonary tuberculosis when the infants were 4 and 9 months respectively. The former infant was breast fed, and the latter slept with her mother.

There was no case of clinical tuberculosis among the 12 patients who received BCG vaccine, 9 of them were immediately separated from their mothers, and only 3 were kept in close contact.

The study suggests that isolation of infants until the mother's sputum is negative for tubercle bacilli and until she is considered to have inactive disease may not be enough to prevent infection in the infant.

F. H. Young

VAN ZWANENBERG, D. **The Influence of the Number of Bacilli on the Development of Tuberculous Disease in Children.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 31–44. [73 refs.]

This paper examines the contacts of patients diagnosed as having pulmonary tuberculosis at the East Suffolk and Ipswich Chest Clinic between January 1st, 1949 and December 31st, 1960. The criteria for inclusion as an index case were a recent chest X-ray examination showing pulmonary tuberculosis, and a sputum test; the patient must have been living in a normal household.

Of 341 index cases with sputum positive for tubercle bacilli by the Ziehl-Neelsen technique, 305 child contacts were examined. Of these, 200 (65·6%) were tuberculin positive and 71 had pulmonary lesions which later showed calcification. 4 of these have since developed post-primary tuberculosis. Of 171 patients who either had no sputum or whose sputum was negative for tubercle bacilli by the Ziehl-Neelsen technique, but who had positive cultures from sputum or laryngeal swabs, 136 child contacts were examined. 35 (25·7%) were tuberculin positive, but only 2 had pulmonary lesions which later showed calcification. Of 227 index cases whose sputum was negative by all methods, 167 child contacts were examined. 35 (21%) of these were tuberculin positive, and 4 had pulmonary lesions which later showed calcification. A detailed criticism of the methods adopted is given.

This is followed by an interesting discussion on the factors involved in contracting tuberculosis, other than the number of bacilli to which the children are exposed. As it is fairly clear that the number of bacilli in the sputum determines whether it is found to be positive on smear or on culture only, there seems every reason to believe that the number of bacilli to which the children are exposed has an influence on the number infected, and the number who develop disease.

[For an earlier study by the author, see this *Bulletin*, 1955, v. 30, 1050.] *F. H. Young*

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 195. **Expert Committee on Tuberculosis. Seventh Report. Geneva, 28 September–3 October 1959.** 19 pp. [Refs. in footnotes.] 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

The Expert Committee on Tuberculosis of the WHO met in September 1959. Its task was to review the WHO tuberculosis control programme. The Committee emphasized that with the progress made in the control of malaria, tuberculosis is now conceded to be the most important communicable disease in the world.

In many countries, particularly those where the tuberculosis problem is greatest, no reliable data exist for measuring the problem. In such countries therefore surveys are required including estimation of the prevalence of persons excreting tubercle bacilli, mass radiography surveys and tuberculin surveys.

Local epidemiological studies should be made to determine in which population groups there is a high incidence of the disease and how it is being spread. The possible role of bovine and other animal infection should not be overlooked.

The Mantoux test with 5 TU of a well-standardized tuberculin is recommended, and the Committee held that in areas where small reactions are infrequent a reaction of 5 mm. or more in diameter may still be used to separate those infected with the tubercle bacillus from those not so infected. In areas where small reactions are common it can only be stated that (1) a reaction of less than 5 mm. indicates in all probability that the person is *not* infected with *Myco. tuberculosis*; (2) a

reaction of 10 mm. or over indicates in all probability that a person is so infected; and (3) a reaction of 5–9 mm. indicates that the person may or may not be infected. A person with a reaction of 10 mm. or more should be examined carefully and periodically for the presence or development of tuberculous disease.

The Committee felt that radiation hazards from chest X-ray examination are negligible compared with its benefits; fluoroscopic screening is however undesirable. Whether or not only tuberculin reactors should be examined in mass X-ray surveys must depend on the local situation.

There is a lack of X-ray apparatus which is sufficiently sturdy, portable or mobile and sufficiently simple to use and maintain, and manufacturers should persevere in seeking to design more suitable plants. The Committee recommend that the 70-mm. mirror-optics camera be used.

The direct examination of sputum for tubercle bacilli is at present the most practical method in many countries but efforts should be intensified to find simpler culture techniques and a practical serological test for determining the presence of active tuberculosis.

The Committee recommended that BCG vaccination should have an important part in the tuberculosis programme of most countries according to the local situation. With a low incidence of the disease mass vaccination is unnecessary and may be confined to selected groups.

Primary chemoprophylaxis—the use of anti-tuberculosis drugs in non-reactors—is not advised; the prophylactic measure of choice for these is BCG vaccination. Secondary chemoprophylaxis—the use of specific drugs in reactors who have no pathognomonic signs or symptoms of tuberculosis and have not recently been vaccinated with BCG—is recommended in areas of high prevalence and generally for reactor children under 4 years of age who have not recently been vaccinated with BCG.

With a view to increasing more rapidly the number of tuberculous persons under specific treatment in all countries the Committee recommended a drug regime for patients being treated in hospital or at home. It would include the daily administration of isoniazid and a companion drug which in ambulatory and domiciliary patients would be PAS. If the choice has to be made between giving isoniazid alone or no specific treatment at all the Committee does not hesitate to say that treatment with isoniazid alone would constitute an acceptable practice at present and until further evidence to the contrary is produced.

The total daily dosage of isoniazid should be 5–10 mgm./kgm. and of PAS 10 gm. The treatment should continue uninterrupted for 6 months after sputum conversion and in no case for less than 1 year. If the patient continues to discharge tubercle bacilli and no changes in management are possible isoniazid may be continued indefinitely with more benefit than harm.

The functions of WHO in the world tuberculosis programme embrace international assistance to individual countries, the training of personnel to replace doctors and nurses in BCG vaccination, radiography, laboratory work, home visiting and health education. Research and the dissemination of information are also important parts of the programme, and the Committee felt that the emphasis should be on field or epidemiological research at present. [This report is a good example of WHO discharging its duty of disseminating information.]

H. G. Calwell

CROFTON, J. **Tuberculosis Undefeated.** *Brit. Med. J.* 1960, Sept. 3, 679–87, 18 figs. [28 refs.]

WHO has calculated that there may be 12–25 million persons in the world with infectious tuberculosis. The number with respiratory tuberculosis in England and Wales has been put at 375,000, of whom some 45,000 are infectious. It is thus clear that tuberculosis is far from being defeated even in highly developed countries.

The chief instruments for the elimination of the disease are mass radiography, chemotherapy and BCG vaccination; in underdeveloped countries vaccination may be the most important tool for some time to come. The resistance of a community can also be improved non-specifically by raising the standard of living, and infectors can be made less dangerous by reducing overcrowding.

The value of BCG vaccination has been established in Great Britain but its value may vary according to the epidemiological situation and it must therefore be applied to suit the circumstances.

Mass radiography may be used for community surveys (in many of which the yield is not worth the effort), in examining high incidence groups such as those with symptoms, adult contacts, prisoners, mental patients, elderly men, hospital in-patients and perhaps contacts of reactor children and in examining " danger " groups such as school-teachers, others in contact with children, bus conductors, shop workers, barmen, doctors and dentists. The mass radiography policy must be kept under continuous review.

The combination of daily streptomycin and isoniazid is almost certainly the most effective form of treatment. The relapse rate falls with the duration of the course, and in Crofton's series it was virtually nil in patients treated for 18 months or more. Sputum conversion is the rule with good treatment.

Techniques of testing for drug resistance are inadequate in many centres, and there is " a chaotic variation " in methods of testing. In Crofton's opinion the only way of establishing the critical level of drug resistance is by comparing the progress of patients with the results furnished by the bacteriologist. The problem of drug resistance is an important one as the figures reported by the International Union Against Tuberculosis show—42% of previously treated and 6·5% of untreated patients with bacillary resistance to at least 1 drug and 5·5% and 0·2% respectively to all 3 drugs.

Crofton thinks there is at present little place in Great Britain for chemoprophylaxis.

The Edinburgh figures for mortality and morbidity are presented; the dramatic improvement they show over the past few years is attributed to good team work and scrupulous chemotherapy. Crofton eschews complacency including that of the administrator " who in some areas may conduct a campaign of attrition on the facilities and morale of the tuberculosis service ".

H. G. Calwell

WALLACE, J. M. **The Effect of a Mass Radiography Campaign.** *Med. Officer.* 1960, Sept. 30, v. 104, No. 14, 208–10.

In 1948 there were 280 notifications of respiratory tuberculosis in Aberdeen (population in 1951, 182,729). The number fell thereafter so that the annual average in the period 1954–56 was 212.

In 1957 there was a mass radiography campaign, and 75·6% of those whose attendance was sought were examined. In consequence the number of cases notified in 1957 rose to 318 but the number in 1958 was only 99.

It was considered that the effect of the campaign would be seen in 1959, and the notifications of that year were studied in detail. There were 116 respiratory and 15 non-respiratory local cases. Of the 116 patients with respiratory disease only 97 had been eligible for and able to attend for X-ray examination in the 1957 campaign. 60 of these had attended, 17 had been X-rayed elsewhere about the same time and 20 had not been X-rayed.

Of the 97 eligible for examination in 1957, 59 had minimal disease, 34 had moderately advanced and 4 had advanced disease. It was seen that if a person had been X-rayed in 1957 and developed tuberculosis in 1959 his disease was more likely to be minimal and if he had not, it was more likely to be advanced or moderately advanced.

The number of contacts of the 116 patients with respiratory tuberculosis who were X-rayed amounted to about 80% of the total number known. 12 were found to have tuberculosis (9 children and 3 adults) and 1 child contact died. Proportionately, patients not X-rayed during the campaign gave rise roughly to 10 times as many secondary cases of tuberculosis as did patients who had been X-rayed at that time. This is another indication of the extent of protection afforded to the community by a mass radiography campaign.

H. G. Calwell

BANG, H. O. & STRANDGAARD, E. **Continued Studies on the Problems of PAS Dosage.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 2, 81–96, 17 figs. [24 refs.]

After pointing out that it has not yet been decided whether PAS is best used in the form of acid proper, or in the form of the salts, the authors discuss the use of the so-called massive dose, the entire 24-hour dose (usually of sodium PAS) being administered at the same time. This affords concentrations considerably higher than any other method of dosage. The literature on this form of treatment is discussed briefly.

In 1958, PAS-IDO calcium granulate, 12 or 9 gm., or the so-called aminosalyl-sodium solution 90 ml. (containing 12 gm. sodium PAS) was administered after breakfast. Broadly speaking, the authors consider that their experience in about 115 cases has been favourable, and many patients, especially the men, like this form of administration. The blood levels following the administration of single massive doses were investigated: 330 specimens from 28 patients treated with PAS-IDO calcium granulate, and 132 specimens from 11 treated with aminosalyl-sodium solution. They found a rapid increase in the blood level up to values between 10 and about 20 mgm. per 100 ml., followed by a rapid fall. However, 8–12 hours elapse until the concentration drops to 2–3 mgm. per 100 ml.

No firm conclusion has been arrived at on the value of phenyl-PAS. Various authors differ on the value they attach to this drug.

A new compound known as Tebanyl compound has recently been introduced. This is powder containing 3 gm. phenyl PAS and 1 gm. PAS. It is administered in the form of a powder 3 times daily in connexion with the 3 chief meals.

27 patients have been treated with this preparation. Most of them had tried several other PAS preparations, but had been unable to tolerate them. It was found that about half the patients could tolerate this drug without difficulty. In 19 the blood levels were studied, a total of 420 specimens. It was found that they varied very considerably from less than 4–5 mgm. to 10–12 mgm. per 100 ml., and in 1 patient about 15 mgm. in the evening.

Preliminary evaluation of the Tebanyl compound suggests that it is a preparation tolerated by a number of patients who cannot tolerate other PAS preparations, and affords blood levels which are on the whole slightly lower than those obtained with calcium and sodium PAS, and sometimes fluctuating capriciously. The authors consider that this preparation may be of considerable value. A number of graphs are shown to illustrate these points.

F. H. Young

PAPANICOLAÖU, B. **The Extra-Sanatorial Drug Treatment of Pulmonary Tuberculosis in the Amman TB Centre, Jordan.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 2, 128–39.

This paper describes the methods by which drug treatment of pulmonary tuberculosis has been carried out at the Amman Tuberculosis Centre, Jordan, under the general direction of WHO. The treatment has been carried out mainly at the patients' own homes, at first with isoniazid alone at 3 mgm./kgm., and later with the same dose of isoniazid combined with PAS 6 gm., daily for adults. It was found that the 6 gm. of PAS were generally adequate and presented few of the difficulties experienced when larger doses were given. 10,135 patients were examined and tuberculous lesions were found in 1,547, of these 642 had active pulmonary tuberculosis, and 75 pleurisy. 221 patients without pulmonary X-ray pathology were treated prophylactically. Of the 642 patients suffering from active pulmonary tuberculosis only 407 (63·4%) attended regularly for treatment. The considerable difficulties met with in ensuring regular attendance are explained. Of the patients who attended regularly, 63 had primary tuberculosis, of whom 45 showed marked improvement at the end of the observation period. In 109 cases of newly diagnosed reinfection tuberculosis, 77 showed marked improvement. Of the old cases of reinfective tuberculosis only 7 of 235 showed marked improvement. The results in pleurisy were excellent, and among the patients submitted to chemoprophylaxis no cases of pulmonary tuberculosis developed.

The author considers that hospital treatment should be limited to the treatment of acute pulmonary tuberculosis, to chest surgery, and to cases resistant to isoniazid and PAS. *F. H. Young*

BELL, W. J. & BROWN, P. P. **Ambulatory Chemotherapy of Pulmonary Tuberculosis in West Africans following Short-Term Hospitalisation.** *West African Med. J.* 1960, Aug., v. 9 (n.s.), No. 4, 153–62, 1 fig. [22 refs.]

This investigation was confined to adult male African patients in Ghana, suffering from acute or subacute pulmonary tuberculosis involving more than 1 lung zone, who had not received specific treatment for more than 14 days previously and who were expectorating acid-fast bacilli which were sensitive to the drugs used.

Those admitted to the trial were allocated randomly to 1 of 2 groups:

Group SPH: streptomycin 1 gm., isonazid 300 mgm. and PAS 12 gm. daily for 12 weeks in hospital followed by PAS 12 gm. and isoniazid 300 mgm. daily for 3 months as out-patients;

Group SH: streptomycin 1 gm. and isoniazid 300 mgm. daily for 12 weeks in hospital followed by isoniazid 300 mgm. and PAS 12 gm. daily for 3 months as out-patients.

There were 159 patients, 78 in the SPH group and 81 in the SH group. 56 were lost sight of during the period of treatment; 2 of them had died. Both groups were comparable in all relevant respects.

After 3 months there was little difference in the degree of clinical or radiological improvement in the 2 groups. Sputum conversion occurred more frequently in the SPH group than the SH group at the end of 3 months but some 30% of all patients left hospital still expectorating tubercle bacilli.

At the end of 3 months more than half the cavities in each group had diminished in size. There was no change in about 10% and an increase in size in about 5% in each group. At the end of 6 months' treatment 33% of the SPH group and 19% of the SH group had closed or blocked cavities; about 10% in each group showed no change or increase in size of cavities.

Apart from differences in the bacterial content of the sputum and in the behaviour of cavities, progress was parallel in the 2 groups during the period of out-patient treatment.

It was concluded that both regimens could reasonably be expected to be effective in bringing about improvement but prevailing factors, particularly the high defaulter rate, must seriously limit the ultimate usefulness of the definitive chemotherapy of pulmonary tuberculosis in West Africa. *H. G. Calwell*

QUANTRILL, J. R. **Experience in the Treatment of Pulmonary Tuberculosis in Africans in Salisbury.** *Central African J. of Med.* 1960, June, v. 6, No. 6, 260–64, 2 charts.

This study comprises 118 African patients in Southern Rhodesia who were treated for pulmonary tuberculosis in hospital and followed up as out-patients. There were 80 males and 38 females, and the largest single group was of males aged 20–30 years.

The basic hospital treatment (6–8 months) was: streptomycin, 1 gm. daily for 30 days, an interval of 30 days, another 30 daily injections, another interval of 30 days and then a final 30 daily injections giving a total of 90 gm. of streptomycin; isoniazid, 5 mgm./kgm. daily for 2 months followed by 10 mgm./kgm. daily for the rest of the stay in hospital; PAS, 1 gm./5 kgm. daily for the whole period.

Patients with pellagra were given a supplement of yeast; when peripheral neuritis occurred isoniazid was stopped and pyridoxine and yeast given. The daily diet amounted to 3,500 calories for adults, including 1 pint of milk.

The average duration of stay in hospital was 6·8 months. Sputum conversion occurred on average in 3·6 months in 76 patients admitted consecutively. The average gain in weight was 18 lb.

Toxic peripheral neuritis occurred in 12 patients of whom one also had a psychosis. All but one were cured or improved within 8 weeks. Toxic reactions to streptomycin and PAS occurred in an unspecified number of patients.

It is the rule to discharge patients when the sputum has been negative for 12 consecutive weeks (direct examination), when the erythrocyte sedimentation rate is below 15/1 (Westergren) and when there is radiological clearing of the pulmonary lesions.

Further treatment and supervision were afforded at a clinic but many patients failed to attend, and the 118 patients studied are those who cooperated.

A supply of isoniazid and PAS sufficient for 2 weeks and 2 lb. of skimmed milk powder were given to each patient attending. X-ray and bacteriological examinations were made monthly or at other intervals, and the aim was that drug treatment should continue for at least 18 months after discharge.

The patients attended on average 3·6 times per year. The PAS test of the urine was positive in a very high percentage; the largest number of negatives was in children. 12 patients relapsed of whom only 4 were taking the drugs regularly. *H. G. Calwell*

i. AMERICAN TRUDEAU SOC. **Chemotherapy of Extrapulmonary Tuberculosis in Adults. A Statement of the Committee on Therapy** [WIER, J. A., Chairman]. *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 441–2.

ii. ——. **Treatment of the Adult Tuberculin Converter. A Statement of the Committee on Therapy** [WIER, J. A., Chairman]. *Ibid.*, 443–5. [15 refs.]

iii. ——. **Treatment of Tuberculosis in Children. A Statement by the Committee on Tuberculosis and Respiratory Diseases in Children** [SMITH, Margaret H. D., Chairman]. *Ibid.*, 446–8.

These 3 papers are taken from the interim report on the drug treatment of pulmonary tuberculosis by the American Trudeau Society.

i. Antibacterial chemotherapy is recommended for all patients with active tuberculous infection. Chemotherapy should be intensive and uninterrupted. Details of treatment follow those usually put forward by instructed American opinion. The chemotherapy should be continued for a prolonged period—usually 2 years—and at least 1 year after the tuberculosis has become inactive. Surgical treatment is ordinarily delayed for several months, and sometimes a long course of preliminary treatment obviates the need for surgery.

Weight-bearing joints usually require surgical fixation, and the fusion of tuberculous joints is best delayed until medical treatment has diminished the soft tissue reaction. Tuberculous lymph nodes often resolve completely under antimicrobial treatment without surgery. Abscesses should be evacuated and occasionally resected. Renal tuberculosis demands very prolonged medical treatment in all cases, but opinion as to what constitutes an indication for nephrectomy is hotly debated.

Tuberculosis of the female genital tract frequently requires surgery in addition to chemotherapy.

In miliary tuberculosis and tuberculous meningitis there is growing evidence that the adrenal corticosteroid hormones are beneficial. Intrathecal therapy is now rarely used in the treatment of tuberculous meningitis.

ii. Various authors say that 5–15% of tuberculin converters develop tuberculosis in one form or another. There is considerable evidence that the administration of antimicrobial treatment to tuberculin positive children and to patients with tuberculous pleural effusions may very significantly alter the ultimate prognosis. On the evidence at their disposal the authors consider that antimicrobial treatment may profitably be given to those who are recent converters, and especially those who are thought to be unusually susceptible to tuberculosis; to those known to have had unusually heavy or prolonged exposures to tuberculosis; and to those in whom unusual circumstances would indicate every precaution in preventing clinical tuberculosis.

It is thought that in many cases the use of isoniazid alone may be sufficient, and in the usual cases it would seem that any disadvantage is less than that produced by the use of PAS. It is emphasized that the place of antimicrobial therapy in the management of the recent tuberculin converter is not yet finally established.

iii. It is considered that isoniazid should always be used. Dosage of about 15 mgm. per kgm. daily is adequate. The addition of PAS is usually recommended in a dose of 200 mgm. per kgm. per 24 hours. Streptomycin is not normally used. Newer antituberculous drugs have no place in the treatment of tuberculous children. The use of corticosteroids should be used for the infant or young child who is dangerously ill in order to support him until antimicrobial drugs have an opportunity to produce some effect.

Therapy should be continued for a least 1 year, and in more severe cases up to 24 months.

The paper then deals with types of disease. In endothoracic primary tuberculous complex enlarged mediastinal glands often produce segmental involvement. When an endomural granuloma is the cause of obstruction bronchoscopic removal of it may hasten the re-aeration of the segment involved.

Tuberculous meningitis should be treated by triple-drug therapy. The proper duration of therapy in cases of meningitis is unknown, but it would appear that treatment should be continued for 1 year, and in most cases for very much longer. Renal tuberculosis usually requires the use of all 3 drugs.

In superficial lymphadenopathy the preferred treatment is drug therapy, which may be followed by local excision. Therapy should extend for at least 12 months.

In tuberculosis of the bones and joints the main problem is the prevention of weight-bearing, and only now and then will prolonged immobilization be necessary. Treatment always includes isoniazid, sometimes with PAS, which should continue for 18 to 24 months in all cases.

When pulmonary tuberculosis of the adult type occurs in children the treatment should be more or less the same as in adults, but thoracoplasty must be avoided at all cost.

In cases of the tuberculin converter without manifest disease, drug treatment should be used in all cases which are known to have developed their tuberculosis in the preceding 12 months. *F. H. Young*

i. SIMPSON, D. G., NASH, Eleanor S. & MCCLEMENT, J. H. **Kanamycin. I. Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 11–22, 4 figs. [30 refs.]

ii. FROST, J. O., HAWKINS, J. E., Jr. & DALY, J. F. **II. Ototoxicity.** *Ibid.*, 23–30, 5 figs. [23 refs.]

i. 36 patients were treated, divided into 3 groups. In group 1, containing 17 patients, observation of the toxic effects of the drug and the study of microbial resistance were the chief objectives. All patients had previously been treated and were assumed to harbour tubercle bacilli resistant to the 3 standard drugs. The dosage of kanamycin ranged from 10 to 30 mgm. per kgm. of body weight, and the duration of the treatment was 10 to 18 weeks. In the 2 other groups evaluation of the therapeutic efficacy was the chief objective. Group 2 consisted of 7 patients, all with active, previously untreated disease with an acute component in all cases, far advanced in 6 and moderately advanced in 1. They received 15 to 23 mgm. per kgm. of body weight daily, and therapy was continued for 6 to 17 weeks. Group 3 contained 12 patients. All had active, previously untreated disease. They were given 12 to 26 mgm. per kgm. of body weight 3 times weekly. Alternate patients, namely 6, also received PAS, 15 gm. daily.

In group 2 no satisfactory improvement was recorded. Treatment had to be stopped prematurely in all patients because of evidence of developing ototoxicity. Some radiological improvement was found in 5 patients, and the sputum of 5 patients became negative for tubercle bacilli on microscopy. The sputum of 2 patients persistently contained tubercle bacilli on culture. Of the 12 patients on intermittent therapy in group 3, 9 completed the prescribed course; the treatment of 2 patients was not completed and one left the hospital. 2 of the kanamycin patients had a moderate degree of improvement as shown by serial X-ray examinations, and 4 had

evidence of the progression of the disease. In all 6 kanamycin-PAS patients there was evidence of X-ray improvement. Tubercle bacilli were shown to have disappeared from the sputum of 2 kanamycin patients by microscopy after 6 and 10 weeks of treatment, and in all 6 of the kanamycin-PAS patients after 4 to 8 weeks. Tubercle bacilli continued to grow on culture in the sputum of all the kanamycin patients; in 2 of the kanamycin-PAS patients tubercle bacilli could no longer be isolated on culture. After the course of kanamycin, treatment with a combination containing isoniazid was continued in all of the patients in groups 2 and 3; substantial improvement was found. At the end of treatment, bacilli in 6 patients in the whole series were completely resistant. Case histories of 3 patients are given.

21 of the 24 patients receiving daily kanamycin were studied. Impairment of hearing was detected in 17 of them after a total of 32 to 134 gm.; the other 4 had no impairment at the end of therapy. Of those on intermittent therapy there was impairment of hearing in 2 only. Tinnitus was common. Transient eosinophilia was common, and transient proteinuria was found in half the patients in whom this had not been present before treatment, and granular casts were found in the urine in every case. These complications were much less marked in patients on intermittent therapy.

The authors conclude that a definite effect was observed on many patients who had previously been untreated, but the earlier loss of microbial susceptibility and the common occurrence of ototoxicity strictly limit the usefulness of the drug in the treatment of pulmonary tuberculosis.

ii. 7 of the 14 patients in group 1, 4 of the 7 patients in group 2, and 6 of the 12 patients in group 3 had normal audiograms at the beginning of treatment; the remainder showed a loss of hearing, usually of a mild degree. The incidence of ototoxicity was closely related to the amounts of the drug administered.

In group 1, 12 of the 14 patients, group 2, 5 of the 7 patients, group 3, 2 of the 12 patients showed significant ototoxicity. The first frequency involved in all patients was 8,000 cycles per second. When the drug was continued the other frequencies were involved in descending order. Hearing loss was present in all but 2 of the patients examined. 13 of the patients reported definite tinnitus, but 4 of these reported a definite improvement within 4 to 8 weeks after the discontinuation of the kanamycin. Mild to moderate nephrotoxic effects of kanamycin have been observed by almost all clinical investigators. It was found that ototoxicity was much more likely to occur where there was impaired renal function.

F. H. Young

SCHNEEWEISS, J. & POOLE, G. W. **Hyperuricaemia due to Pyrazinamide.** *Brit. Med. J.* 1960, Sept. 17, 830–32, 4 figs. [16 refs.]

These authors from the Hammersmith Chest Clinic and the Postgraduate Medical School, Hammersmith Hospital, London, have confirmed an observation, originally made in the United States, that the administration of pyrazinamide causes a rise in the blood uric acid. In several patients referred to in the original report and in one of these authors, actual manifestations of gout resulted. The material reported here consists of 6 patients treated with 2·5 gm. pyrazinamide daily (because of resistance of their tubercle bacilli to drugs of first choice) together with one other drug. Charts referring to 4 of them show steep rises in blood uric acid produced by pyrazinamide and corresponding falls in urinary excretion of uric acid. It is also shown that this effect can be reduced by also giving probenecid.

L. P. Garrod

WOLFART, W. Ruft Isonikotinsäurehydrazid Tumoren hervor? [**Does Isoniazid cause Tumours**] *Deut. med. Woch.* 1960, Sept. 9, v. 85, No. 37, 1655–7. [24 refs.]

The finding of extensively scattered metastases in a patient with bronchial carcinoma who had been treated with isoniazid (total dose 7·8 gm.) because the condition had been diagnosed as tuberculous led to speculation about the possibility that isoniazid may be carcinogenic. A considerable amount of experimental work has been done on the question, and many of the experiments are recounted in detail in this paper. No confirmed evidence emerges of any carcinogenic effect of isoniazid, and where tumour formation occurred it could have been due to impurities in the preparation of the drug used. Wolfart has examined histological sections of the lungs of tuberculous patients treated for long periods with isoniazid and has failed to find any pre-cancerous changes.

If isoniazid were carcinogenic its excretion by the kidneys might be expected to lead to a rising incidence of bladder cancer in patients undergoing treatment for pulmonary tuberculosis, but in fact the coincidence of pulmonary tuberculosis and carcinoma of the bladder in 2 series of patients fell from 4·9 to 1·4% after the introduction of isoniazid.

A reported increase in the incidence of lupus-carcinoma is attributed by Wolfart to the effect of isoniazid in promoting fibrous tissue formation since malignant changes might take place later in such tissue.

Should there be in the future an increased incidence of lung tumours in patients with pulmonary tuberculosis treated with isoniazid it should be attributed to a malignant growth of fibrous tissue. There is as yet no confirmed evidence that isoniazid is carcinogenic and no certain proof that it is not. Further experimental work is required.

H. G. Calwell

YANG, G. **Resection and Concomitant Thoracoplasty in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 45–50. [10 refs.]

This paper reports the results of 137 cases of resection and concomitant thoracoplasty among a total of 348

resections in the treatment of tuberculosis. The operations were carried out between February 1953 and August 1958.

The 60-day post-operative mortality was 3·6%, and there has only been 1 late death from tuberculosis. The author considers that this mortality could be further reduced as the result of experience. Overall 60-day mortality among 348 patients who had resections performed during the period was 1·7%. It was considered that 38·7% were poor risk, 51·1% average risk, and 10·2% good risk patients. The technical procedures are detailed. A table is given of the post-operative complications, but only 2 patients had bronchopleural fistulae and empyemata. In a follow-up of 6 months to 2 years 83·2% of patients were alive with inactive disease.

In the discussion the author considers the reasons for adopting this method of treatment. *F. H. Young*

PYLE, Marjorie M., LANGSTON, H. T. & PFUETZE, K. H. **Chemotherapy in Resection for Pulmonary Tuberculosis. Problems of Extensive Disease and Drug-Resistant Organisms.** *Amer. Rev. Respiratory Dis.* 1960, July, v. 82, No. 1, 51–8.

This paper deals with all patients subjected to pulmonary resection at the Chicago State Tuberculosis Sanitarium during a period of 4½ years. The total number was 358 patients, 112 of whom had extensive resections, including 75 pneumonectomies. Of these, 100 patients (29%) had problems of chemotherapy owing to resistance of antituberculous drugs in various combinations, or had positive sputum at the time of operation. The various combinations of antituberculous drugs which were given are detailed, but as patients were treated as individual cases statistical information on the various numbers could not be given.

1·7% of the 358 patients died within the post-operative period of 60 days or less. The cause of death in 2 was gastrointestinal haemorrhage, post-thoracotomy bleeding in 1, pulmonary infarction in 1, cardio-respiratory insufficiency in 1, and uraemia in 1 case. Post-operative tuberculous complications occurred in 5·4% of the 358 patients. At a date nearly 5 years after the first and six months after the last resection 88·2% had inactive disease. It was reckoned that 5% represented therapeutic failures.

In the group of 258 patients who did not present problems of chemotherapy only 2 had tuberculous complications, and both of these had strains of tubercle bacilli resistant to streptomycin and isoniazid and, in retrospect, should have received ancillary medication. Cycloserine was found very useful in rendering patients with chemotherapeutic problems ready for operation. The problems of chemotherapy proved far more important than the extent of resection in the production of tuberculous complications.

The authors conclude that by the judicious use of all chemotherapeutic agents, many patients with extensive disease, and those who have organisms resistant to streptomycin and isoniazid, can be treated successfully by resectional surgery. *F. H. Young*

BRITISH MED. J. 1960, Oct. 1, 979–86, 4 figs. **Freeze Dried B.C.G. Vaccine. Stability of the Vaccine under Different Conditions of Storage and Persistence of Tuberculin Sensitivity in Schoolchildren after Vaccination. Second Report to the MEDICAL RESEARCH COUNCIL by their Committee on the Standardization of Freeze-Dried B.C.G. Vaccine** [EVANS, D. G., Chairman].

In a preliminary investigation by the Medical Research Council [this *Bulletin,* 1958, v. 33, 335] it was found that British freeze-dried BCG vaccine (Glaxo) was as constantly viable as fresh Danish vaccine and produced satisfactory tuberculin conversion rates in vaccinated children. As the batches of vaccine used had been stored continuously in the refrigerator it was considered advisable to make further investigation into the stability of batches stored at different temperatures and for various periods.

Laboratory tests of stability were made by determining the number of viable bacillary particles in both dried and liquid vaccine. In each study the viable count of vaccine removed at intervals from storage at 4°C. was compared with that of vaccine stored at room temperature (average 23°C.) and at 37°C. for periods up to 63 weeks, and batches stored at 4°C. and 45°C. for shorter periods. A batch was also examined frequently during 155 weeks of storage at 4°C.

It was found that the level of viable count at 4°C. remained almost constant over a period up to 65 weeks. Storage at room temperature was followed by a fall in viable count amounting to 3–8-fold in 36–60 weeks. One individual batch was found to be less stable than the others.

Fall in viability count at the higher temperatures occurred rapidly during the early period of storage at both 37° and 45°C. At 32°C. however the counts were similar to those obtained with storage at 4°C., no fall being evident over the 78-hour period.

Clinical trials were made by vaccinating 2,642 children who had reacted to 100 TU with induration of less than 5 mm. They were allocated to various vaccine groups at random.

Post-vaccinal tuberculin testing with 3 and 100 TU was done 1–4 months after vaccination when all the children except 2 were found to have undergone tuberculin conversion. The conversion rates to 3 TU were 95·2% with liquid vaccine, 85·3% with refrigerated dried vaccine and 77·5% with dried vaccine stored at room temperature. There were some variations between different batches; for example one batch gave a low conversion rate despite its high viable count.

The mean diameter of the post-vaccinal Mantoux reaction was 13·6 mm. with liquid vaccine, 11·9 mm. with refrigerated dried vaccine and 11·7 mm. with dried vaccine stored at room temperature.

The vaccination lesions were inspected, also at 1–4 months. The mean diameter was 9·5 mm. with liquid vaccine, 8·3 mm. with refrigerated dried vaccine and 8·4 mm. with dried vaccine stored at room temperature. No complications of vaccination were reported.

Reactor rates on retesting at 10–13 months were analysed. The percentages reacting to 3 TU were 92·1,

85·0 and 79·8 respectively. These results support the conclusion reached at 1–4 months. There were differences between individual batches.

The relationship between viable counts and post-vaccinal conversion rates was studied. In some cases the results were anomalous, and this may have been due to ampoule-to-ampoule variation arising from the unstable nature of the batch.

In view of the fact that post-vaccinal tuberculin sensitivity may be affected by repeated tuberculin testing a group of vaccinated children were tested at 12 months after vaccination only. Considering all vaccines together the conversion rates to 3 TU were 76·9% compared with 77·0% in children tested both at 1–2 and 12 months. For all vaccines together the mean diameter of tuberculin reactions was 11·7 mm. for those tested only at 12 months compared with 12·3 mm. for those receiving 2 tests; the difference was not significant. It was thus shown that the results obtained at 12 months were a true indication of post-vaccinal tuberculin sensitivity.

It was concluded that British freeze-dried BCG vaccine is satisfactory but care must be taken in its handling during storage and transit. It seems advisable not to store it at temperatures over 4°C. although a temperature of approximately 20°C. for short periods of up to 1 week would be unlikely to cause much deterioration. In view of the differences found between batches, tests of accelerated degradation before issue may be advisable. Such a test is being investigated.

H. G. Calwell

BHUSHAN, K. **Assessment of BCG Vaccination in India. Third Report.** *Indian J. Med. Res.* 1960, July, v. 48, No. 4, 407–17, 1 map & 1 graph. [11 refs.]

The BCG vaccination campaign now covers all the States of the Indian Union. By the end of 1958 more than 120 million persons had been tested with tuberculin and 42 million of these vaccinated.

Continuous appraisal of post-vaccinal tuberculin sensitivity has been made since 1955, based on the retesting of groups of vaccinated schoolchildren. In the absence of adequate control groups unvaccinated children in the same schools were tested at the same time for comparison. The Mantoux test with 5 TU of PPD was used.

In the period 1955–58 the assessment team retested 18,367 children vaccinated in the mass campaign in 262 schools in 129 different localities as shown on a map. The children had been vaccinated with 91 different batches of vaccine produced in Madras. The interval between vaccination and retest varied from 1½ to 42 months.

The mean size of reactions varied from 8·3 to 16·6 mm. with a mean of 12·5 mm. Less than 10% of the mean values were under 10 mm. and less than 10% over 15 mm.

In order to judge whether groups with mean size of reactions between 10 and 15 mm. to 5 TU may be considered to have achieved a satisfactory level of post-vaccinal sensitivity the degree of sensitivity was also examined in children classified as positive in the campaign and those classified as negative who had refused vaccination. It was found that vaccination had been responsible for an increase of 6–7 mm. in the mean size of reactions and the degree of sensitivity of the vaccinated group was 6–7 mm. less than that of the naturally infected children.

The distribution of the vaccinated groups by mean size of reaction was analysed. One-third had their sensitivity increased by 1–6 mm. and two-thirds by 7–11 mm. Compared with what can be considered the highest attainable degree of sensitivity under controlled conditions one-third fell short by 5–9 mm. whereas two-thirds were within 4 mm. of this level.

H. G. Calwell

COMSTOCK, G. W. & SHAW, L. W. **Controlled Trial of BCG Vaccination in a School Population. Tuberculosis Studies in Muscogee County, Ga.** *Pub. Health Rep.* Wash. 1960, July, v. 75, No. 7, 583–94, 1 chart. [22 refs.]

This controlled trial of BCG vaccination in Georgia was begun in 1947. The participants were Negro and white schoolchildren who had failed to react to 100 TU of PPD with at least 5 mm. of induration. These non-reactors were divided into 2 groups by the year of birth; 1 group was vaccinated and the other left unvaccinated.

6 months after vaccination 70% of the vaccinated children were retested with 5 TU and 100 TU of PPD. 45% reacted to 5 TU and 93% to 5 or 100 TU. Non-reactors to 100 TU were revaccinated.

Cases of tuberculosis among the study population were identified through the normal tuberculosis service, and it was considered very unlikely that any were missed. No effort was made to examine each participant individually.

There were 11,262 children whose pre-vaccinal 5 TU tests were read at 48 hours; their average age was 11·4 years. 1,492 (13%) reacted to 5 TU, 3,768 (33%) reacted to 100 TU, and 422 were unclassified because of refusal to accept vaccination or medical contra-indication to it. 2,498 were vaccinated and 2,341 were controls.

Repeated Mantoux testing of controls in 1950 and 1957 showed average annual infection rate of 0·2% in white and 0·7% in Negro children.

In the 12-year period to 1959 there were 35 persons with definite tuberculosis first diagnosed after the trial began. 28 had pulmonary and 7 non-pulmonary disease. There was bacteriological confirmation in 20. 24 of the patients had been reactors to 5 TU, 2 non-reactors to 5 TU but not tested with 100 TU, 5 had reacted to 100 TU, 2 had been vaccinated and 2 were unvaccinated controls.

Initially neither of the 2 vaccinated children who developed tuberculosis had any reaction to 100 TU of PPD. 6 months after vaccination 1 had still no reaction to 100 TU. He was revaccinated and after this showed 15 mm. of induration to 100 TU; in 1950 he had 4 mm. of induration to the 5 TU test. The other subject had

12 mm. of induration to the 5 TU test 6 months after vaccination but was not tested in 1950. These cases occurred in the 8th and 10th years.

The results are compared with those of the Medical Research Council's trial in England [this *Bulletin,* 1960, v. 35, 253]. The marked disparity in the rate of protection demonstrated suggests that the risk of infection must have been many times higher in Great Britain than in Georgia. "This has a direct bearing on the need for vaccination in the two areas, since it seems obvious that the need for vaccination varies directly with the likelihood of becoming infected." *H. G. Calwell*

VENEREAL DISEASES

GINTSCHEFF, P. Z. Sudanrot-Cholesterin-Kristalle als Antigenträger und ihre Anwendung in der Serodiagnose der Lues. [**Use of Sudan Red Cholesterol Crystals as Antigen Carrier in the Diagnosis of Syphilis**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 568–75, 4 figs.

If a solution of cholesterol and the dye Sudan III is prepared in alcoholic ox-heart extract and while boiling has cold physiological NaCl solution sprayed into it, fine needle-like mixed crystals of cholesterol and Sudan III are formed which absorb the lipoid present in the heart extract.

If a mixture of the crystal suspension so obtained is mixed with normal human serum there is no change but where an inactivated syphilitic serum is added the crystals clump and precipitate out leaving a supernatant which is stripped of complement-fixing antibody and has become Wassermann negative.

The flocculation reaction only happens in the absence of complement but the interfering action of that substance can be eliminated by addition of "Liquoide" Roche as well as by the usual heat inactivation. Full details are given of the preparation of heart extract, crystal suspension and liquoid solution and of the necessary technique in carrying out the test in fluid mixtures mounted between slide and coverslip, or in capillary tubes, and observed with the naked eye.

Comparative results of Wassermann reaction and crystal agglomeration test are recorded for 5,901 sera. All those positive to this Wassermann reaction were positive by the new test. A group of 881 persons, presumably non-syphilitic, blood donors, pregnant women, etc. gave negative results with both tests. The group of latent, treated and doubtful syphilis gave 148 positive with the new test although Wassermann negative. [If fully corroborated these results indicate a valuable advance in the laboratory diagnosis of syphilis.] *J. W. McLeod*

BEKKER, J. H. De klinische interpretatie van de moderne serologische reacties bij de diagnostiek van syfilis. [**The Clinical Interpretation of Modern Serological Tests for the Diagnosis of Syphilis**] *Nederl. Tijdschr. v. Geneesk.* 1960, Oct. 1, v. 104, No. 40, 1935–7.

The English summary appended to the paper is as follows:—

"The author discusses the clinical interpretation of modern serological tests used in diagnosing syphilis, viz., the Treponema pallidum immobilization test and the Reiter protein complement-fixation test.

"These tests, especially the immobilization test, are so specific that a positive result is practically proof of contact with *T. pallidum,* but it provides no evidence on the activity of a pathological process, if any. The sensitivity of these tests, in particular that of the Reiter protein test, is such that a negative test almost excludes the possibility of an active infection, unless the infection was acquired very recently."

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

REIMANN, H. A. **Spectrums of Infectious Disease. A Review, with special reference to Inapparent and Mild Infections.** *Arch. Intern. Med.* 1960, May, v. 105, No. 5, 779–815, 23 figs. [185 refs.]

Although mild cases of the major infectious diseases have long been recognized, it is only since 1919, when NICOLLE described "inapparent infection" in experimental rabbit typhus, that attention has increasingly been focused on graded degrees of severity in infectious diseases. Advances in diagnostic techniques have been the means of sorting out mild forms of many infections which could not be distinguished from one another clinically. Coxsackie and ECHO virus infections, for example, have been distinguished from poliomyelitis (especially non-paralytic cases with meningitis), and the same applies to those forms of histoplasmosis and coccidioidomycosis which simulate tuberculosis. Mild yellow fever can now be differentiated from influenza, viral hepatitis, dengue and malaria. These advances

have cleared up much confusion in epidemics, have made statistics of incidence and mortality much more accurate, and have led to logical prophylaxis and therapy. Moreover, textbook descriptions of "typical" cases are now seen to be misleading in that they often represent the exception rather than the rule; and untreated inapparent and mild cases assume a new importance, clinically because they may lead to major complications or chronic states (a missed case of diphtheria or brucellosis for example), and epidemiologically because they may spread infection widely.

The author has constructed from available data spectrum bars for various infections; these show the relative proportions of (a) uninfected persons; (b) inapparent, (c) mild, (d) moderately severe, (e) severe, and (f) fatal cases. The spectra vary greatly. At one extreme lie poliomyelitis, viral hepatitis, mononucleosis, Q fever, brucellosis, and others, whose inapparent and mild forms far outnumber severe and fatal ones; in these the spectra are almost filled with the bars (b) and (c). In contrast, pneumococcal lobar pneumonia and cholera, being usually severe, have spectra largely composed of bars (d) and (e). At the other extreme is rabies, which is always fatal with a spectrum represented entirely by the (f) bar. But other factors enter the picture—for example type 1 pneumococcal pneumonia differs from type 3, and primary tuberculosis differs from the reinfection variety.

Statistics and spectra are never static; they depend on one set of circumstances at a given place and time. But with increasing knowledge more accurate spectra may be designed, and may give a truer view of the overall effects of a particular infection. *H. Stanley Banks*

TWOHIG, J. N. **The Zoonoses—Some Epidemiological Aspects.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Aug., v. 19, 128–31.

This paper outlines very briefly some of the principal epidemiological features of the zoonoses, with reference to the second report of the Joint WHO/FAO Expert Committee [this *Bulletin*, 1959, v. 34, 1002]. After a short account of the principal implications of the zoonoses the author underlines the close relationship between human and animal health. Until comparatively recently the medical and veterinary sciences were concentrated on their own immediate needs; veterinary public health is now an adjunct to veterinary medicine and the two sciences have become more closely related: doctors and veterinarians are now more than ever aware that both have a special part to play in the furtherance of public health.

A table lists 10 common zoonotic diseases, their causative agents, commonly accepted animal reservoirs and modes of infection.

The development of control measures is referred to, but the author points out that animal control is not enough. "There is need for the continued education of the public towards a more discriminative attitude in dealing with animal contacts and animal products and towards the maintenance of high standards of hygiene in all that pertains to food."

There is also a need for constant integration of effort and co-operation between general practitioner, public health official, epidemiologist, veterinarian, laboratory worker and hospital physician if the zoonoses are to be kept under control. *H. J. O'D. Burke-Gaffney*

SEGA, A., RENZI, G. & BUZZONI, L. Aspetti clinici delle neuroassiti virali nel Riminese. Considerazioni su 126 casi. **[Clinical Aspects of Viral Infections of the Nervous System in the Rimini District. Observations on 126 Cases]** *Giorn. di Malattie Infettive e Parassit.* 1960, May–June, v. 12, Nos. 5/6, 244–9, 2 figs. [30 refs.]

This series of 126 cases was spread over a period of 24 years. In 56 of the patients the disease took the form of acute lymphocytic meningitis which followed a benign course and 36 of these cases were in 1955. 31 others had encephalitis and 4 meningo-encephalitis. Myelitis or meningo-myelitis was the form in 7 others and radiculoneuritis in 6. Besides these "primary" viral neuraxites there were 22 other cases (17·4% of the series) where the condition had followed an attack of measles or parotitis or vaccination against smallpox or rabies.

The authors believe that the "primary" cases may have been due to Coxsackie virus. *J. Cauchi*

SPINK, W. W. **Adrenocortical Steroids in the Management of Selected Patients with Infectious Diseases.** *Ann. Intern. Med.* 1960, July, v. 53, No. 1, 1–32, 22 figs. [19 refs.]

Infections may prove hazardous to a patient in two main ways—peripheral vascular failure due to shock may occur, or the inflammatory reaction to infection may itself prove harmful. The author considers these groups separately. In the first group, 38 patients suffering from a variety of infections—25 being of the coliform-*Pseudomonas-Proteus* group—are studied: all were treated with the usual therapeutic procedures (antibiotics, infusions, pressor agents, oxygen) and in addition large doses of adrenocorticosteroids were given. 23 of the 38 patients died. Many of the patients were elderly, 13 of the "coliform" group being over 70, and suffering from a variety of other serious conditions, *e.g.* gangrenous cholecystitis. The author insists on high dosage—300–500 mgm. of hydrocortisone intravenously every 8–12 hours for 2–3 days. He claims that the adrenal glands in these cases are not impaired but that their maximum production of corticosteroids is insufficient to meet the stress of overwhelming infection. There is little danger in a short course of high dosage and in some cases of peripheral vascular failure recovery seemed clearly due to this treatment.

The corticosteroids are often dramatically effective when the inflammatory process itself seems to be harmful to the patient. In infectious mononucleosis, in mumps complicated by orchitis or encephalitis, in some tuberculous conditions, in purpuric states due to infection, in brucellosis, rheumatic fever, hepatitis and a variety of other infections the administration of the

drugs may alter the course of the disease within 24 hours. In severe drug reactions, *e.g.* severe penicillin allergy with thrombocytopenia and encephalitis, the corticosteroids are often highly effective. When the corticosteroids are given in very high dosage for only a few days there is no need to taper off the dosage gradually—the drug can be stopped when the effect has been obtained. [This article is recommended for careful study by all clinicians.]

[See also this *Bulletin,* 1958, v. 33, 309.]

A. B. Christie

HANSKY, J. **Acquired Agammaglobulinaemia.** *Med. J. Australia.* 1960, Aug. 6, v. 2, No. 6, 220–21, 1 fig.

A woman, aged 26, suffering from recurring chest infections was found to be suffering from agammaglobulinaemia, 0·008 gm.% compared with the normal 0·9 to 1·1 gm.%. Immune tolerance studies in the rabbit confirmed the virtual absence of gamma globulin from the patient's serum. She was Mantoux positive and had had measles and rubella as a child without undue disturbance. Both her children had normal amounts of gamma globulin in their serum. There was no evidence of myeloma, nephrosis or reticulosis in the patient and her agammaglobulinaemia was therefore regarded as of the primary acquired type. She was treated, not with gamma globulin, but with tetracycline 250 mgm. twice daily and this appeared to keep her free from infections.

A. B. Christie

HOSPITAL AND OTHER CROSS INFECTIONS

HARDYMENT, A. F., WILSON, R. A., COCKCROFT, W. & JOHNSON, Betty. **Observations on the Bacteriology and Epidemiology of Nursery Infections.** *Pediatrics.* Springfield, Ill. 1960, May, v. 25, No. 5, Pt. 2, Suppl., 907–27, 1 fig.

(I) *Staphylococcal Skin Infections.* The incidence of pyodermia in infants in the nurseries of the Vancouver General Hospital was studied over a 9-year period, the second half of which was divided into 7 experimental periods of between 1½ and 18 months.

Initially the infection rate was 12% and this was not consistently lowered by improved nursing techniques and the introduction of 1% ammoniated mercury ointment for the babies' skin. In the experimental periods the authors used combinations of hexachlorophene (G11) to the infants' skin in bath water or lotion and green soap or G11 in various preparations for nurses' hands.

The best results were obtained when G11 was used in detergent in babies' baths and for nurses' hands over an 18-month test period (VII) when the infection rate was 0·26%. When the babies' skin was untreated the rate was 4·42% in spite of G11 treatment for the nurses' hands.

There was no direct relationship between pyodermia rate and nasal carrier state of adult contacts. The infant nasal carrier rate fell to 4% during period VII. Although at subsequent samplings under similar conditions the infant carrier rate was 15% and 29% the overall carriage rate of mothers (about 30%) was unaffected by the length of stay in hospital although the resistance rate to penicillin and chlortetracycline rose.

There was no consistent relationship between staphylococcal air counts and the pyodermia rate. Staphylococci were recovered from the hands and bedding of about one-third of the mothers but only from 4% of babies' blankets when G11 was used. Organisms were not recovered from nurses' hands when G11 was used but gowns were found to be contaminated.

(II) *Incidence and Bacteriology of Conjunctivitis Related to Different Methods Used in Prophylaxis of Ophthalmia Neonatorum.* To study the incidence of conjunctivitis over an 18-month period babies were divided into 3 groups. One group received silver nitrate and one group penicillin into the eyes and a 3rd group was untreated. Conjunctivitis due to staphylococci was practically eliminated during the second half of the test period during which time all babies were receiving G11 baths; that from which other organisms or no organisms were isolated was the same in both periods. During the whole period fewer cases occurred in the penicillin group than either of the others. As G11 baths practically eliminated the staphylococcal conjunctivitis and as penicillin was not strikingly superior in infection due to other organisms the authors recommended that silver nitrate should remain the prophylactic agent against gonorrheal ophthalmia.

(III) *Bacterial Contamination of the Umbilicus.* In spite of G11 baths the umbilical carrier rate of staphylococci was about 78% and of haemolytic streptococci 83% on one occasion when the pyodermia rate was low. This carrier rate was not lowered by treatment of the cord with Zephiran. Painting the cord with triple dye [this *Bulletin,* 1957, v. 32, 900] however lowered the rate to 6% for staphylococci and 9% for haemolytic streptococci.

(IV) *Follow-up Survey.* Follow-up visits to 2,790 babies born in the 9 hospitals in the Vancouver area and a few born at home showed that skin infection after discharge from hospital ranged from 3·7% to 11%. It was generally lower in babies born in a hospital using G11 in some form than in hospitals in which this treatment was not given.

M. Patricia Jevons

ROTTINGHUIS, H. & HUYSMANS-EVERS, A. G. M. Staphylococcus aureus in het ziekenhuis. Het probleem in het algemeen, en in het bijzonder in de Verloskundige Kliniek. [***Staphylococcus aureus* in the Hospital. The Problem in General, and in Particular in the Maternity Hospital**] *Nederl. Tijdschr. v. Geneesk.* 1960, June 11, v. 104, No. 24, 1140–46, 1 fig. [26 refs.] English summary.

The author has studied the incidence of staphylococcal infections in a maternity hospital in Amsterdam. The investigations were carried out in 1958, and included 100 pregnant women attending the ante-natal clinic, 102

parturient women, 103 newborn infants, and the entire nursing and medical staff.

Coagulase-positive staphylococci were isolated from the nose in 33 pregnant women, and 29 of the strains were sensitive to antibiotics. Among the staff the incidence of penicillin-resistant staphylococci was around 70%; 8 of 88 strains isolated were of phage-type 80/81. At the time of delivery 33 strains were isolated from the 102 mothers, and the number rose to 41 after 5 days in hospital and to 53 after 10 days; 6, 6 and 9 strains were resistant to penicillin at the 3 times respectively; 1 strain was also resistant to streptomycin, but all strains were sensitive to tetracycline and erythromycin. 2 strains were of phage-type 80/81. 101 of the 103 infants became infected with coagulase-positive staphylococci, which could be isolated from the nose, hands and umbilicus, and on discharge 34%, 59% and 32% of the infants harboured penicillin-resistant strains in the 3 sites respectively.

The wearing of masks had no apparent effect upon the incidence of staphylococcal infection in the mothers and their infants. From a questionary sent out 3 months after discharge, to which 97 mothers replied, it was found that 5 women had suffered from mastitis and 4 infants had suffered from a skin infection. It is pointed out in conclusion that the presence of phage-type 80/81 in the hospital did not give rise to an epidemic. *Anne Tothill*

Biro, L., Gibbs, R. C. & Leider, M. **Staphylococcal Infections. A Study of Incidence on a Dermatologic Ward.** *Arch. Dermat.* 1960, Aug., v. 82, No. 2, 205–11.

Of 306 patients admitted to the dermatology service of the Bellevue Hospital, New York, in a 9-month period, 27 (8·8%) developed some staphylococcal disease. The percentage incidence was: 2·6% in 192 patients having neither antibiotic nor corticosteroids; 7·3% in 41 having antibiotics; 11·9% in 42 having steroids; and 45·1% in 31 having both. The primary diseases suffered by the patients in the treatment categories differed considerably so that the role of the treatment cannot be fully assessed. Most of the infections seemed to develop about 2 weeks after the patient's admission to hospital. 5 patients died, all aged 60 or more; 4 had pemphigus vulgaris and one mycosis fungoides as the underlying disease. *R. E. O. Williams*

COCCAL INFECTIONS

The order in this section is:—***Staphylococcus, Streptococcus, Neisseria, Others.***

Holland, W. W., Tanner, Elizabeth I., Pereira, Marguerite S. & Taylor, C. E. D. **A Study of the Aetiology of Respiratory Disease in a General Hospital.** *Brit. Med. J.* 1960, June 25, 1917–22, 5 figs. [14 refs.]

An extensive clinical, virological, and bacteriological study was made of cases of acute respiratory disease admitted to, or occurring in St. Thomas' Hospital, London, during the winter of 1958–59; 28% of these illnesses in children and 22% in adults were found to be associated with an identifiable virus—most commonly during this period that of Influenza A or B. The bacteriology of the sputa showed *Streptoccocus pneumoniae* in 36% of specimens examined, *Haemophilus influenzae* in 22%, and *Staphylococcus aureus* in 2%. The death rate, wholly in adults, was 6·7%.

A new strain of *Staph. aureus* was acquired by 24% of the children and 33% of the adults during their stay in hospital, and 84% of these strains were resistant to penicillin, and most of them to more than one antibiotic.

The investigation did not reveal what was hoped for—an association between particular clinical syndromes and different aetiological agents. *H. Stanley Banks*

Hinton, N. A., Taggart, J. G. & Orr, J. H. **The Significance of the Isolation of Coagulase-Positive Staphylococci from Stool. With special reference to the Diagnosis of Staphylococcal Enteritis.** *Amer. J. Clin. Path.* 1960, June, v. 33, No. 6, 505–10. [16 refs.]

Faeces were examined for coagulase positive staphylococci in an attempt to assess the significance of this organism and to aid the diagnosis of staphylococcal enteritis.

Stool samples were examined from 425 patients suspected of having infectious intestinal disease and from 747 controls, who fell into 5 groups: normal adults; members of hospital staff with no history of recent antibiotic treatment; patients with no history of intestinal disease, and newborn infants.

A direct film was examined and 1 gm. of the specimen was emulsified in saline and plated on blood agar and Difco staphylococcus medium 110. Plates were examined after 48 hours and numbers of staphylococci isolated were roughly graded.

The isolation rate was 13·8% in normal adults and 17·1% in patients with no enteric disease. The latter group included a few more strains resistant to antibiotics. Carriage rate in hospital staff was 23·7%, and the higher number of resistant strains reflected the hospital contact. 23·1% of adult patients with diarrhoea were positive soon after admission, many of these patients had had antibiotics and many strains were antibiotic-resistant. 42·5% of the 80 patients with diarrhoea who had been in hospital more than 4 days carried staphylococci, in 3 this was the predominant organism. 17·5% of these patients carried strains resistant to tetracycline, and 12·5% to erythromycin.

The carriage rate, the weight of infection and the resistance rate in infants under a year were higher than in adults and were related to hospital contact and administration of antibiotics.

In 19 patients (6 adults, 9 infants and 4 newborn) staphylococci could be seen in direct films and isolated on non-selective media. All these patients had diarrhoea and 14 of them had had antibiotics to which the strain was resistant on isolation. 2 of the adults and 1 infant died and pseudomembranous enteritis was demonstrated at autopsy.

The authors concluded that a diagnosis of staphylococcal enteritis is unlikely with negative cultures but that a positive culture is of little diagnostic significance unless the organism is present in large enough numbers to be seen in direct films and isolated on non-selective media.

[It would be interesting to know how the phage types of strains isolated from the hospital patient with diarrhoea compared with strains from the hospital staff and from enterotoxin-producing strains from food poisoning.] *M. Patricia Jevons*

JOHNSON, Eloise E., STOLLERMAN, G. H., GROSSMAN, B. J. & MCCULLOCH, H. **Streptococcal Infections in Adolescents and Adults after Prolonged Freedom from Rheumatic Fever. I. Results of the First Three Years of the Study.** *New England J. of Med.* 1960, July 21, v. 263, No. 3, 105–11, 2 figs. [19 refs.]

While the administration of continuous antibiotic prophylaxis in rheumatic patients is now accepted practice, there is considerable doubt regarding the necessary duration of such prophylaxis. The authors studied the effect of stopping prophylaxis and, instead, treating only clinical infections in a group of 298 adolescents and adults who had been free from rheumatic symptoms for at least 5 years. Asymptomatic infections were detected by throat cultures and serum antibody estimations every 2 months. The authors found a marked drop in infection rates after the age of 18. The infection rates in adolescents (12 to 22 years) was 23·2% and in adults (23 to 70 years) 12·8%. In the adolescent group there were 7 recurrences per patient year, in the adult group none. The authors do not consider that their findings are a sound basis for modifying present prophylactic practice. Stopping prophylaxis in the adult remains a calculated risk that must be assessed for each individual patient. *A. B. Christie*

CHAMOVITZ, R., RAMMELKAMP, C. H., Jr., WANNAMAKER, L. W. & DENNY, F. W., Jr. **The Effect of Tonsillectomy on the Incidence of Streptococcal Respiratory Disease and its Complications.** *Pediatrics.* Springfield, Ill. 1960, Sept., v. 26, No. 3, Pt. 1, 355–67, 2 figs. [29 refs.]

"A population of military men with acute streptococcal respiratory infections (diagnosis established by clinical, bacteriologic and serologic studies) was investigated. Evidence is presented indicating that individuals who have had a tonsillectomy are neither more nor less susceptible to acute streptococcal infections of the respiratory tract. Once individuals acquire a streptococcal infection, the clinical course of the acute illness is not modified appreciably by the presence or absence of the tonsils. However, if antibiotic therapy is withheld, suppurative complications occur less frequently in those patients who have had their tonsils removed.

"Tonsillectomy did not alter significantly the attack rate of acute rheumatic fever as a sequel of streptococcal infections, nor did it reduce significantly the development of valvular heart disease in patients with acute rheumatic fever. Moreover, it appears that streptococcal infections are less readily recognized in tonsillectomized patients and, therefore, are more likely to escape treatment appropriate for the prevention of rheumatic fever."

VOLLUM, R. L. & JUEL-JENSEN, B. E. **Treatment of Respiratory Infection in Schoolboys with Phenethicillin.** *Brit. Med. J.* 1960, Oct. 1, 994–5.

Phenethicillin (Broxil) was given to 31 boys in a preparatory school suffering from respiratory infections due to Group A beta haemolytic streptococci. The clinical results were satisfactory. Serum penicillin levels were equal to those expected after parenteral administration of penicillin G. Absorption was rapid but fell to very low levels after 4½ hours. The dose given to the majority was 250 mgm. every 4 hours during the day, but none during the night. *A. B. Christie*

ANDERSON, T. B. **Pneumonia with Antibodies to Streptococcus MG.** *Lancet.* 1960, June 25, 1375–8, 1 fig.

In this article by a general practitioner, and based on a thesis for M.D. Cambridge, an attempt is made to explain the significance of a rising titre of *Streptococcus* MG antibodies in some cases of primary atypical pneumonia. What the author calls "*Streptococcus* MG pneumonia" is a complication of a minor acute-respiratory illness. The incubation period of the pneumonic complication is probably 2–3 weeks. There may be rigors at onset, development of breathlessness, pain in the chest, cough, and sputum; râles are usually heard in the chest and there is a patchy opacity in the radiograph. The white-cell count is low, normal, or slightly raised. There is little sign of nasopharyngeal inflammation by the time that pneumonic signs appear. The course lasts for 2 weeks or more, and secondary bacterial pneumonia with much mucopurulent sputum may further complicate the illness.

This form of atypical pneumonia is associated with the production of antibodies to *Streptococcus* MG; they reach a maximum in the second week or later. This organism belongs to the group *Str. salivarius,* and is generally non-pathogenic. It is commonly found, however, as an invader in atypical pneumonia associated with Eaton agent (as shown by rising antibody titres) [this *Bulletin,* 1960, v. 35, 676, 790], and the suggestion is that *Streptococcus* MG has a pathogenic function in this type of pneumonia. The diagnosis can be made by a general practitioner on the basis of the clinical picture and of the presence of *Streptococcus* MG antibodies. *H. Stanley Banks*

SPINK, W. W. & SU, C. K. **Persistent Menace of Pneumococcal Meningitis.** *J. Amer. Med. Ass.* 1960, Aug. 6, v. 173, No. 14, 1545–8.

The authors review the management of pneumococcal meningitis, basing their views on a series of 55 patients.

Penicillin is the drug of choice and should be given systemically in very large doses—1,000,000 units intravenously per hour till improvement occurs; thereafter in equivalent doses by intramuscular injection. With these doses intrathecal administration of penicillin is unnecessary. Sulphonamides may be used in addition and the place of steroids requires more investigation. The commonest source of infection is the middle ear. Mortality was 25% in the whole group, but 53% [8 deaths in 15 patients] in those over 40. Residual damage is often severe and recurrent attacks are not uncommon.

A. B. Christie

TING, Tsai-Tao, YIN, Ch'üan-Min & WANG, Huei-Chen. **Short Course of Sulfonamide Treatment in Epidemic Meningococcus Meningitis: an Analysis of 1,363 Cases.** *Chinese Med. J.* Peking. 1960, Apr., v. 80, No. 4, 356–62, 2 figs.

The following points are brought out by this study:
(1) Sulphonamides are the treatment of choice for meningococcal meningitis; the case fatality rate in this series of 1,363 children of all ages under 14 years was 1·92% (excluding the considerable number of patients dying within 24 hours of admission).
(2) Sulphathiazole was as efficacious as sulphadiazine and was associated wits haematuria only in 2% of 92 patients compared with 13·5% of 1,224 treated with sulphadiazine [see also BANKS, this *Bulletin*, 1941, v. 16, 215].
(3) During an epidemic it may be convenient, and is probably safe, to give a short course of the drug of about 3 days; among 701 patients so treated there was no death and no known relapse.
(4) Penicillin is a valuable adjunct in cases complicated by pneumonia or arthritis, and where steroids have to be used, as in fulminating meningococcal septicaemia.

H. Stanley Banks

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

WAGENHALS, C. O. & TANNENBERG, J. **Outbreak of Typhoid Fever Starting with a Case of Purulent Meningitis.** *J. Amer. Med. Ass.* 1960, May 28, v. 173, No. 4, 355–9. [18 refs.]

Typhoid meningitis is a rare complication of the bacteriaemia of typhoid fever. In the case described, a man of 33, meningeal signs were observed on the fifth day of the disease. The spinal fluid contained several thousand white cells, mainly polymorphonuclears. *Salmonella typhi* type E1 was grown both from the fluid and from blood samples taken at the same time as the lumbar puncture. Treatment with chloramphenicol (plus penicillin until the diagnosis was confirmed) brought the infection under control within a few days, but not before an excitable period with delirium and confusion had occurred—probably a Herxheimer type of reaction.

Epidemiological enquiry showed that the patient had been infected by drinking water contaminated from a near-by septic tank. The septic tank had been contaminated during a temporary stay in the house of a carrier of *Salm. typhi* E1. The organism was cultivated from the well water by running samples of 250 ml. and 750 ml. through a bacteria-tight filter. *H. Stanley Banks*

SHAMMA'A, M. H. & GHAZANFAR, S. A. S. **D-Xylose Test in Enteric Fever, Cirrhosis, and Malabsorptive States.** *Brit. Med. J.* 1960, Sept. 17, 836–8, 1 chart. [21 refs.]

The pentose D-xylose is normally not present in man and presumably for that reason is relatively unaffected by metabolic processes. Yet, like most sugars, it is predominantly absorbed from the small intestine, more in the proximal than in the distal part. Whereas the absorption of most sugars involves phosphorylation it is doubtful whether xylose is absorbed in that way. The absorption of xylose has been used as a test for numerous diseases of the small intestine and in this study, from the American University Hospital, Beirut, Lebanon, the D-xylose excretion test has been employed in enteric fever and liver cirrhosis. 25 gm. of xylose were given by mouth and urine was collected for 5 hours. The amount of urinary xylose was then determined by a colorimetric method (ROE and RICE, *J. Biol. Chem.*, 1948, v. 173, 507). Of 13 patients with proven enteric fever 9 had a lower urinary excretion of xylose than the lowest in the authors' control group of 11 medical students and a few patients with no disease of the gastro-intestinal and renal tract. 9 of 14 patients with cirrhosis of the liver also had lower xylose excretions than the lowest seen in the control group. There was a correlation between low serum albumin level and low xylose absorption. *H. Lehmann*

PASCU, Alexandrina, MOTOC, R. & TENGHEA, P. Febra tifoidă. Relații între tratament, recăderi si starea de purtător. **[Typhoid Fever. Relationship between Treatment, Relapses, and the Carrier State]** *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, July–Aug., v. 5, No. 4, 331–40, 1 chart. [31 refs.]

The English summary appended to the paper is as follows:—

"In 741 cases of typhoid fever the authors have studied various types of chloramphenicol treatment and their results as regards relapses and the occurrence of germ carriers.

"The most efficacious treatment was found to consist in prolonged administration of small doses of chloramphenicol (1–1·5 g per day) for a period of at least 14 days following the subsidence of fever. By this means the incidence rate of relapses was reduced from 21·6%

to 13·6% and the incidence rate of carriers from 31·3% to 21%.

"The authors emphasize the advantages of this method and particularly its epidemiological importance."

HU, Hsiu-Yuan, TSENG, Ch'ing-Sheng, HSÜ, Chih-Nan & YING, K'uei-Sheng. **Antibody and Agglutinin Response to TAB Vaccination.** *Chinese Med. J.* Peking. 1960, June, v. 80, No. 6, 554–61.

The TAB vaccine used in the tests described in this paper contained 500 million typhoid bacilli and 250 million paratyphoid A and B bacilli respectively per ml. No other information is given about its composition or method of preparation. The paper is concerned with a comparison of the immune response in volunteers, as assessed by the production of agglutinins and mouse-protecting antibodies against a virulent challenge for each component, inoculated either by the subcutaneous or intradermal routes with different dose schedules.

The agglutinin responses in the different groups one month after the completion of vaccination were not significantly different, whether the dose was 0·5, 1·0 and 1·0 ml. or 0·25, 0·5 and 0·5 ml. subcutaneously, or 3 doses of 0·1 or 2 doses of 0·15 ml. intradermally. In all cases the interval between the injections was 7 days. The mouse-protection tests indicated that the best results were obtained with the subcutaneously administered vaccine in half the standard dosage (*i.e.* 0·25, 0·5 and 0·5 ml.). It is not quite clear whether the booster dose (the same dosage as the last of the primary injections) was given at 6 or 12 months after the first series, but, as would be expected, the sera collected 1 month after the booster dose showed enhanced responses. The response to vaccination against paratyphoid B was less satisfactory than with the other components. The mouse-protection is considered to be more sensitive than the measurement of agglutinins, and the results more helpful in evaluating the immune response to TAB vaccination.

H. J. Bensted

SZTURM-RUBINSTEN, S., CHAMFEUIL, R., HUET, M. & MENANTAUD, J. A propos d'une culture de *Sh. sonnei* isolée de glace alimentaire. [**Studies on a *Shigella sonnei* Strain isolated from Ice**] *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 456–8.

The English summary appended to the paper is as follows:—

"The origin of the contamination in two cases of *Sh. sonnei* dysenteria was demonstrated by the epidemiological survey. A strain was isolated from the ice used in the patients' food: it possessed the same biochemical properties and belonged to the same phage-type as the strains isolated from the patients' stools.

"The observation shows the importance for epidemiological surveys of two characters of *Sh. sonnei*: the capacity of attacking xylose and the phage-type."

WALLIS, H. R. E. ***Brucellosis in England.***

This book was reviewed on p. 1256.

KHAIKINA, B. G. **The Relations of the Allergy Test with Serological and Bacteriological Tests on Brucellosis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 8, 109–13. [Translated from Russian.]

This paper gives an account of brucellin skin tests, agglutination tests and blood cultures on 160 patients suffering from brucellosis classified as acute, subacute and chronic. The brucellin was injected intradermally in 0·1 ml. in 3 dilutions representing 1, 1 in 10 and 1 in 50 skin-test doses.

The author's results show that the brucellin skin test was more often positive in the 1 in 50 dilution when the blood culture was negative. This applied to acute, subacute and chronic cases but it was more marked in the chronic cases and the antibody titres generally ran a parallel course with the results of the skin tests.

It is suggested that the brucellin reaction is closely linked with the protective mechanism, of which the antibody level is an expression of the degree of protection present. Thus low antibody titres and poor brucellin reactions mean absence of immunity or a low degree of immunity so that the organism is able to invade the blood stream from some tissue in the body. Therefore, the brucellin or allergic reaction must be regarded as an expression of the defence mechanism. The author appreciates that this lacks proof but considers that the evidence presented supports his thesis. *H. J. Bensted*

POBEREZKIN, M. N. **Positive Brucellosis in Persons without Clinical Manifestations of Illness.** *J. Microbiol., Epidemiol. & Immunobiol.* 1959, v. 30, No. 6, 123–31. [12 refs.]

This report from Soviet Russia is based on observations made over a period of 7 years on persons who exhibited initially a positive reaction to brucellar antigen without clinical manifestation of illness. 718 were from a focus of *melitensis* (goat-sheep) infection, 537 had been exposed to infection from cattle and 426 were employed in meat factories. In addition, 3,596 persons who had been vaccinated with dried live vaccine were investigated.

A positive reaction is shown to accompany some degree of protection against the effects of further infection. A small proportion of those with a positive reaction in a focus of goat-sheep infection developed clinical brucellosis within the first month after infection (attributed to additional massive infection). Similarly, in those vaccinated, no clinical illness occurred between 2 and 7 months after vaccination. Alimentary infection from cows caused scarcely any illness. A strain of *Brucella abortus* was cultured from the blood of a canteen worker who had had no symptoms and who gave negative serological and allergic [presumably skin] reactions.

Where exposure to infection was for a limited period the reactions disappeared within 1 year in 79% and in the remainder within the next 4 to 5 years. In those employed in the meat factories the reactions persisted for the whole period of observation, *i.e.* 6 to 7 years but no clinical illness developed.

[The strain of *Br. abortus* appears to have been of low pathogenicity. The live vaccine used appeared to give a similar degree of protection against *Br. melitensis* as subclinical infection.] *Frederick J. Wright*

PROC. ROY. SOC. MED. 1959, Feb., v. 52, No. 2, 109–14 (Sect. Epidem. & Preventive Med. 1–6), 4 figs. **Symposium on Tetanus** [BOYD, J.; MACKAY-SCOLLAY, E. M.; CONYBEARE, E. T.].

The incidence of tetanus and its relation to active and passive immunization in 2 world wars is briefly reviewed by Sir John Boyd. The outbreak in Stoke-on-Trent in 1957 when 5 cases of tetanus developed after operations in a theatre block is described by Dr. Mackay-Scollay. 3 possible causes for the outbreak are discussed—the presence of tetanus spores in the wall plaster, contamination of the theatre by a heavily infected arm amputated in the theatre just before the outbreak, and the presence of tetanus spores in unbleached grey cotton wool. The incidence of tetanus in the civilian population of England and Wales and methods to reduce it still further are discussed by Dr. Conybeare.

A. B. Christie

WOODWARD, W. W. **Tetanus Eight Days after Administration of Anti-Tetanus Serum.** *Brit. Med. J.* 1960, Sept. 24, 916.

A woman with incomplete septic abortion was given 1,500 units tetanus antitoxin but 8 days later nevertheless developed tetanus. She had previously had tetanus antitoxin 3 years earlier and this may have led to rapid loss of antitoxin due to sensitization on the second occasion. The author refers to previous cases [this *Bulletin*, 1955, v. 30, 311], to the failure of clinical tetanus to produce lasting immunity, and to the necessity of subsequently actively immunizing against tetanus and diphtheria patients who have been given antitoxin derived from the horse against either condition.

A. B. Christie

PATEL, J. C., DHIWANI, M. K. & MEHTA, B. C. **Cephalic Tetanus.** *Indian J. Med. Sci.* 1960, Aug., v. 14, No. 8, 695–9.

Cephalic tetanus is described by the authors as tetanus complicated by any cranial nerve palsy: in their 22 cases, the facial nerve was the one involved. Mortality in the cases was comparable with the average mortality for tetanus—36% for cephalic compared with 43% for "general" tetanus. [It is important not to confuse cephalic tetanus as defined by the authors with cerebral tetanus.] *A. B. Christie*

YEOH, G. S. **Tetanus. A Review of One Hundred and Thirty Cases seen and Treated in the Surgical Professorial Unit, General Hospital, Singapore.** *Singapore Med. J.* 1960, June, v. 1, No. 2, 59–62, 4 figs.

130 patients suffering from tetanus were treated between 1947 and 1959, and 3 systems of treatment were used. In the first period, 1947–54, patients were given antitoxin, penicillin and paraldehyde; from 1954 to 1957, chlorpromazine, promethazine, and pethidine were added to the treatment; from 1957 to 1959, intravenous polyvinylpyrrolidone (Periston-N) was added, the total dose varying with severity, and up to 300 ml. Periston has a molecular weight of 12,600 and has the property of adsorbing toxin in the blood stream; it is easily filtered through the glomeruli and adsorbed toxin is thus eliminated. The number of patients in the 3 periods were 80, 28 and 22 and the mortality rates 53·8%, 50% and 22·7%. The author feels that under comparable conditions the addition of Periston-N to the treatment reduces mortality substantially. *A. B. Christie*

PERLSTEIN, M. A., STEIN, M. D. & ELAM, H. **Routine Treatment of Tetanus.** *J. Amer. Med. Ass.* 1960, Aug. 6, v. 173, No. 14, 1536–41.

This article, based on the treatment of 300 patients over a period of 25 years, describes the routine treatment of tetanus at Cook County Hospital, U.S.A. Points stressed are the desensitization regime for patients allergic to antitoxin, the care of the patient after tracheotomy, the use of meprobamate and the management of tetanus in heroin addicts. [This is a good descriptive article.] *A. B. Christie*

MENON, K. A. **"Notensil" in the Treatment of Tetanus. Report on a Clinical Trial.** *Med. J. Malaya.* 1960, Mar., v. 14, No. 3, 184–6.

7 patients aged from 2 days to 50 years suffering from tetanus were treated with tetanus antitoxin and a combination of phenobarbitone and Notensil (acetylpromazine). The relaxant effect of this drug is claimed to be nearly 10 times that of chlorpromazine. The drug by itself was not so effective as when given along with phenobarbitone. A satisfactory dose was 2 mgm. per pound body weight per day. *A. B. Christie*

CORNELEAC, V. & FILIMON, Eugenia. Contribuţii la tratamentul tetanosului la nou-născut (4 ani de experienţă clinică). [**Contributions to the Treatment of Tetanus in the Newborn**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, May–June, v. 5, No. 3, 273–6.

The authors have treated neonatal tetanus by the method of BUŞILĂ and POP (*Pediatria*, 1956, No. 4, 353) which consists of continuous narcosis with luminal or phenobarbitone, combined with antitoxin treatment, antibiotics, oxygen, and feeding with mother's milk by stomach tube. Of 27 patients treated by this method in a hospital in Bacău, Rumania, between 1955 and 1958, 11 survived; 5 case histories are presented.

D. J. Bauer

VANDEKERKOVE, M. & LEVIGUELLOUX, J. Difficultés techniques d'apprécier l'importance du réservoir de virus murin dans la leptospirose. [**Technical Difficulties in Estimating the Importance of the Rat Reservoir in Leptospirosis**] *Méd. Trop.* Marseilles. 1960, July–Aug., v. 20, No. 4, 440–46.

The authors discuss various technical difficulties which they met with during an investigation of the leptospiral carrier rate in the rats of Marseilles. If these difficulties are not appreciated, workers may fail to isolate leptospires and thereby draw wrong conclusions.

Rats should be captured alive, not poisoned; they should be killed by drowning since the use of chloroform greatly reduces the number of positive cultures obtained. Each kidney should be cultured, and inoculated into guineapigs, separately: pooling of kidneys reduces the number of positive cultures obtained. Leptospires were never observed by dark-ground microscopy of urine or kidney emulsion.

Guineapigs inoculated intraperitoneally with leptospire-infected material may react in one of three ways. (a) Fever (40°C. or higher) and jaundice, followed by hypothermia (36°, even 34°C.) with haemorrhages, then death—80% of cases (42/52). (b) Fever and jaundice, followed by recovery —2% (1/52). (c) Transient fever (less than 40°C.) between days 4–10 after inoculation, with recovery—17% (9/52). The animals should be kept in separate cages and the temperature should be taken twice daily. Young animals, less than 250 gm. in weight, react better than older, heavier ones. Positive results were obtained from sick guineapigs most frequently (about 50%) when blood obtained in the febrile phase or liver were inoculated into fresh guineapigs or culture medium.

The value of guineapig inoculation as a method for isolating leptospires from other animals is limited: only those organisms pathogenic in guineapigs will be recovered.

Direct culture in a suitable medium should be carried out in parallel with animal inoculation. After various trials a medium containing 10% rabbit serum, 1% haemoglobin, and 1% vitamin B12 (50 μgm./ml.) was adopted.

[No information is given concerning the carrier rate in the rats, or the identity of leptospires isolated. This paper does, however, emphasize the necessity for newcomers to this particular subject to obtain advice or to consult an authoritative text (*e.g.* WOLFF, this *Bulletin*, 1955, v. 30, 86) before they start work.] *L. H. Turner*

POKORNÝ, J. & HAVLÍK, O. Experimentální infekce myšice křovinné (*Apodemus sylvaticus* L.) leptospirou *L. gryppotyphosa*. [**Experimental Infection of *Apodemus sylvaticus* L. with *Leptospira grippotyphosa***] *Českoslov., Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 2, 88–92. English summary.

The authors infected 39 *Apodemus sylvaticus* [the method is not stated in the English summary] with *Leptospira grippotyphosa* and observed leptospires in the blood of 8 of 10 at different intervals in the first 13 days. Serological response was pronounced, the titres reaching 1 in 3,000 to 1 in 30,000, and remaining at those levels for 6 months—and probably for the whole life of the animals. Leptospires were cultured from 8 of 9 animals killed after 1 month, from 4 of 5 killed after 2 months, and from others killed at 3 or 4 months.

The authors discuss the possible role of these animals in maintaining foci of infection. *Charles Wilcocks*

ASMERA, J. *L. grippotyphosa* u zajíce polního. [***L. grippotyphosa* in the Hare *Lepus europaeus***] *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 7, 501–4, 1 fig.

The English summary appended to the paper is as follows:—

"1,035 sera of hares Lepus europaeus were examined serologically for Leptospirae. The materials originated in 43 cedastres of 10 districts of the region of Ostrava. Also 55 isolation trials from kidneys in Korthof's medium and serum water were performed. 11.11% reacted positively with L. grippotyphosa. Reactions with other leptospirae were negative. On the basis of the performed isolation trials, the author succeeded in gaining strains of L. grippotyphosa from two localities. By this finding, it is sufficiently proved that the hare Lepus europaeus meeting on its localities various species of little mammals (Microtus arvalis, Clethrionomys glareolus, Apodemus flavicollis, Apodemus sylvaticus) which are known as reservoirs of leptospirae, has an influence on the persistence of the infective agent in natural foci and so becomes a new reservoir of L. grippotyphosa."

VÁZQUEZ HOYOS, A. & PEREIRA ZAPATA, S. La Kanamicina en el tratamiento de la leptospirosis experimental del cobayo. [**Kanamycin in the Treatment of Experimental Leptospirosis in the Guineapig**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1959, Sept., v. 19, No. 3, 255–8.

The English summary appended to the paper is as follows:—

"1. *Leptospira icterohaemorrhagiae* var. *kantarowicz* is susceptible to the action of Kanamycin "in vivo".

"2. Experimental leptospirosis in the guinea pig can be cured with Kanamycin and the chronic carrier condition never takes place.

"3. No toxicity was found at the dose used in this experiment."

VIRUS INFECTIONS

The order in this section is:—***General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.***

ANGELILLO, B., CALARESU, I. & MASIA, G. F. Sulla frequenza di anticorpi per ornitosi in Sassari e provincia. [**The Frequency of Ornithosis Antibodies in Sassari and Province**] *Igiene Moderna.* 1960, v. 53, Nos. 1/4, 37–41.

The English summary appended to the paper is as follows:—

"A serological investigation has been carried out on the frequency of ornithosis antibodies in Sassari and province.

"In 220 human sera a positivity of the 9·0% was observed. The highest frequency has been encountered in people living in the province (14·0%) and in agricultural labourers (13·1%) respectively.

"Out of 210 bovine sera, 29 (or the 13·8%) showed the presence of ornithosis antibodies."

SĂRĂTEANU, D., NASTAC, E., FUHRER, B., OPRESCU, E., HUA, C. T. & TAO, H. Cercetări comparative asupra valorii diagnostice a reacției de fixare a complementului si intradermoreacției în infecția ornitozică. [**Comparative Investigations of the Diagnostic Value of the Complement-Fixation and of Intradermal Test in Ornithosis**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, May–June, v. 5, No. 3, 253–9. English summary.

The diagnostic value of the complement-fixation and intradermal tests for ornithosis has been studied in rabbits infected with the virus intratracheally, and in 70 agricultural and slaughterhouse workers. The intradermal test with inactivated infected allantoic fluid became positive in the rabbits 9 hours after infection, reaching maximum intensity after 48 hours; the complement-fixation test became positive after 10 days, and antibody could be found up to 35 days after infection. Of the 70 persons investigated 30 gave negative results in both tests, in 21 both tests gave positive results and in 19 the results were not in agreement; positive results were obtained in 51·4% by the complement-fixation test and in only 35·7% by the intradermal test.

D. J. Bauer

VOSS, J. A. Encephalitis vaccinalis i Norge. [**Post-Vaccinal Encephalitis in Norway**] *Tidskr. f.d. Norske Laegeforening.* 1960, Sept. 1, v. 80, No. 17, 801–2. English summary.

The Norwegian vaccination law of 1954 enjoined the vaccination of every child before the end of the year following the year in which he or she was born. In 1955 the Director of the Public Health Service circularized the medical profession with explanatory notes amplifying and elaborating the text of this law. Medical officers of health must teach that, as a rule, the child should be vaccinated between the ages of 3 and 12 months, and that after the age of 2 years no one is to be vaccinated without the definite consent of the parents who, on presenting a child for vaccination after this age must be told of the risks of brain complications. No assistant vaccinator may vaccinate anyone older than 2 years.

Since 1950 there has been a marked fall in the incidence of post-vaccinal encephalitis in Norway, and Voss is inclined to give the restrictions on vaccination after the age of 2 years much of the credit for this fall. In the 5-year period 1945–49 there were 26 cases, and in 18 of them the child had been between 2 and 8 years old when vaccinated. In the 5-year period 1950–54 there were 8 cases, and in 5 of them the child had been over 2 years. In the 5-year period 1955–59 there had been 6 cases, 4 of which had exceeded the 2 years limit. Voss, who is in charge of the Animal Vaccination Department of the State Institute for Public Health, queries the wisdom of vaccinating for the first time men presenting themselves for national service, for of late there have been some cases of encephalitis contracted under these conditions.

Claude Lillingston

BERGER, K. & PUNTIGAM, F. Die Altersdisposition bei postvakzinaler Enzephalitis. [**Age and Postvaccinal Encephalitis**] *Deut. Med. Woch.* 1960, Aug. 26, v. 85, No. 35, 1520–24, 1570. [11 refs.]

This paper reports an investigation of post-vaccinal encephalitis in Upper Austria, Salzburg and Vienna. There were no differences in incidence between these areas, but there were statistically significant differences between age-groups. In the age-group 1–3 years there was about 1 case in 10,000 primary vaccinations. The incidence increased with age: 4–5 years—1 in 2,000 vaccinations; 6–10 years—1 in 650 vaccinations; 11–14 years—1 in 120 vaccinations. The death rate similarly increased with age.

Colin Kaplan

REYNOLDS, E. O. R. **A Fatal Case of Eczema Vaccinatum.** *Lancet.* 1960, Sept. 24, 684–6, 2 figs. [18 refs.]

The patient was a girl, aged 2 years, who had suffered from infantile eczema since she was 3 months old. When her brother was vaccinated no enquiry was made about family history of skin disorder. This vaccination "took"; and the lesion remained uncovered. Some 7–10 days later vaccinia lesions appeared on the eczematous areas of the girl, who became very ill; and in spite of treatment which included hyper-immune gamma globulin she died, having developed a terminal coagulase-positive resistant staphylococcal infection.

This case emphasizes the need for instruction to parents of eczematous children on the danger of contact with vaccinia virus, and the risk of spread of infection from an uncovered vaccinia lesion in the pre-crusting stages.

[Many cases of this nature are on record.]

J. Pickford Marsden

PLEYDELL, M. J. **Anencephaly and Other Congenital Abnormalities. An Epidemiological Study in Northamptonshire.** *Brit. Med. J.* 1960, Jan. 30, 309–15, 4 figs. [14 refs.]

A praiseworthy and very suggestive epidemiological enquiry by a Medical Officer of Health in the unusual field of congenital abormalities is described. This is a model study, showing how the records available to a local Public Health Department can be utilized to shed fresh light on the obscure pathogenesis of these extremely important causes of death and disability. The information was obtained from birth registers, and infant mortality registers, from special records kept by midwives and health visitors, and records of obstetricians, paediatricians, mental health departments, and schools for handicapped children. In this way the incidence of congenital abnormalities in Northamptonshire for the years 1944–57 was obtained, and was found to confirm the data obtained by PENROSE (1955, unpublished memorandum). But the incidence of anencephalic births in urban districts was found to be twice that of rural districts, and in the industrial belt of the county thrice that in the rest of the county; these births were also grouped in categories of time and space. From the Scottish data on stillbirths it was ascertained that there is a distinct seasonal incidence of stillbirths due to anencephaly in the winter months November to February.

It is deduced that these various groupings are best explained on the hypothesis that the condition is the result of maternal infections, especially in the earlier stages of pregnancy. Certain retrospective and prospective enquiries on infections in expectant mothers and mothers after delivery have strengthened the possibility that this explanation is correct, especially in regard to the role of acute respiratory infections, particularly influenza.

If this thesis is confirmed it is clear that much more attention will have to be paid to the prevention of infections in expectant mothers, especially in the first few months of pregnancy—a time when there is still insufficient supervision of the health of the expectant mother. *H. Stanley Banks*

GORBUNOVA, A. S. **An Analysis of the Causes of the Influenza Epidemic Outbreak in the First Quarter of 1959.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 255–8.

In January and February 1959 there was a mixed A2 and B influenza virus epidemic in the large towns of the Soviet Union, in which A2 strains predominated. There were 2 reasons for this epidemic. The first factor was the decrease in immunity to A2 virus during 1958. Thus, haemagglutination-inhibition (HI) studies on 500 sera at the Institute of Virology, Moscow, showed that antibody to the A2 Singapore strain fell from 1:460 at the end of 1957 to 1:60–1:80 at the end of 1958. Reports from the bases of the Regional Influenza Centre for the last 3 months of 1958 also showed a fall in the collective immunity to A2 virus. The second factor was the difference in the antigenic pattern of A2/59 virus from the 1957 strain as shown in cross HI tests [ISACHENKO, this *Bulletin*, 1960, v. 35, 1246] and there was also a change in the antigenic pattern of B virus strains particularly from those of 1949 [SATKHANOVA, *ibid.*, 1247]. *D. Taylor-Robinson*

RISTORI, C., BOCCARDO, H. & BORGOÑO, J. M. La epidemia de influenza asiática en Chile y su repercusión en la mortalidad. [**The Asian Influenza Epidemic in Chile and its Repercussion on Mortality**] *Bol. Oficina Sanitaria Panamericana.* 1960, Aug., v. 49, No. 2, 132–48, 6 figs. [10 refs.] English summary.

An epidemic of influenza produces not only deaths from influenza but also an increased mortality from other causes specially from respiratory diseases. In the pandemic of 1918–20 it is estimated that there were throughout the world, 200,000,000 cases and 12,000,000 deaths. In Chile in those years among a population of 3,000,000 there were 37,500 deaths.

The recent pandemic started in China in the early months of 1957 and caused in Chile 5,400 deaths. The new type of virus was named successively Japanese 305, A Asian-57 and A-2. The infection reached Chile before July 1957. A National Committee was set up and reported in November that the virus was type A Asian-57.

The authors have examined all death certificates for 1956 and 1957 and present numerous tables recording their findings. In 1956 the population of the country was 6,543,629 and the general death rate was 12·8 per 1,000; in 1957 it was 13·7 and in 1958 13·2. A chart gives the total deaths month by month and shows a sharp rise in August and September 1957. There were 5,997 more deaths in August 1957 than in August 1956. Analysis by cause shows that the main increases were in pneumonia and bronchopneumonia, senility and other ill-defined diseases. Of the 3,064 deaths classified to influenza in 1957 2,442 were complicated by pneumonia, 536 by other respiratory conditions, 19 by those of the digestive tract and 67 by involvement of the nervous system. The fall in the death rate from tuberculosis which has gone down steadily from 250 per 100,000 population in 1948 to 56·1 in 1958 was arrested in the winter of 1957 but continued its descent when the influenza departed. The death rate from cancer is rising and there was a peak in the graph in August 1957.

Other tables demonstrate that the death rates were highest in the isolated Southern provinces where the winters are severe and medical services scanty: they also show that the very young and the old suffered the heaviest mortality. It is estimated that at all ages the case fatality was only 0·15%.

Recommendations are that a plan be prepared now to provide adequate medical care should another epidemic occur: that antibiotics effective against staphylococci be kept ready and made available in priority for those over 55 and those suffering from chronic illness. Vaccines, if available in time, should be given to the elderly and to the groups whose absence from work would cause a breakdown in public services.

[The English summary is full and remarkably good.

For an account of the outbreak in Santiago and in Talcahuano see this *Bulletin*, 1958, v. 33, 817.]

Allen Daley

HOULT, J. G. & FLEWETT, T. H. **Influenzal Encephalopathy and Post-Influenzal Encephalitis. Histological and other Observations.** *Brit. Med. J.* 1960, June 18, 1847–50, 6 figs.

The Asian influenza epidemic of 1957 provided an opportunity to study a significant number of the rare cases of major neurological disorder associated with influenza. In 1958 the authors reported 12 such cases [this *Bulletin*, 1958, v. 33, 928]. Six presented neurological symptoms after the acute influenzal attack had subsided, and all but one recovered; the other six were cases of clinical "encephalitis" occurring during the acute attack of influenza, and were all rapidly fatal. The brains of 5 of the latter group have now been studied intensively by means of serial sections; 4 were children aged 5–13 years who died 7–9 days after the onset, and the fifth was a man of 44 who died 11 days after the onset.

In the first 4, only scanty histological changes were found after prolonged search; these consisted of (1) patchy lymphocytic infiltration of meninges and perivascular spaces, and (2) foci of microglial proliferation with loss of Purkinje cells in the cerebellum. These lesions suggested scanty and patchy loss of neuron cells with the resulting repair changes. The fifth case showed the perivascular demyelination and ring haemorrhages characteristic of haemorrhagic leuco-encephalitis, possibly of allergic nature and similar to the post-infective encephalitis following measles and smallpox.

It is concluded that these results, taken in conjunction with the clinical findings in the 6 recovered cases, suggest that there are two main forms of major neurological disturbance following influenza: (1) an acute encephalopathic variety, with minimum histological lesions, occurring early in the attack of influenza, and (2) the post-infective type of demyelinating leuco-encephalitis. [This is a contribution of major importance.]

H. Stanley Banks

CULVER, J. O., LENNETTE, E. H., STEVENS, Thirza E. & NITZ, R. E. **Antibody Response to Influenza Vaccines containing the Asian Strain.** *J. Immunology*. 1960, Aug., v. 85, No. 2, 197–202, 1 fig. [12 refs.]

219 military recruits (California) were randomly divided into 4 approximately equal groups and each group given one of the following preparations: 400 chick cell agglutinating (CCA) units of A2/Japan/305/57 virus in 1 ml. subcutaneously (vaccine I), the same in 2 ml. subcutaneously (vaccine II), an adjuvant polyvalent vaccine containing 150 CCA units of A2/Japan and 50 units each of Swine 31, A/PR8, A1/AA/56 and B/GL/1/54 in 0·25 ml. intramuscularly and, finally, formolized saline in 1 ml. subcutaneously. Influenza was at a low ebb during the 56-day period under consideration.

There was a three-fold and 1·5-fold increase in soluble complement-fixing (CF) antibody to vaccine I and vaccine II respectively, the peak being attained in 10 days and declining slightly over the 56 days of observation. The authors suggest that any further increase after 10 days could be assumed to be due to influenza and such a rise would be most easily detected in those subjects who received vaccine II. It would be more difficult to detect in those who received the adjuvant vaccine for there was a 4-fold CF antibody increase after 10 days and a slight increase over the following 46 days. Determinations of haemagglutination-inhibition (HI) antibody response were made on 25 randomly selected men who received the adjuvant vaccine. When the response was measured with A1/Albany antigen the geometric mean titre increased from 10 to 34 over the 56 days. There was practically no response to the A2/Japan antigen in 9 of the same men but the geometric mean titre in the remaining 16 increased from 14 to 1,650 after 14 days, suggesting, in the latter group, prior experience with A2 virus.

D. Taylor-Robinson

PEREIRA, Marguerite S. & FISHER, O. D. **An Outbreak of Acute Laryngotracheobronchitis associated with Parainfluenza-2 Virus.** *Lancet*. 1960, Oct. 8, 790–91.

Parainfluenza 2 virus was originally called croup associated virus (CA) or acute-laryngo-tracheo-bronchitis virus (ALTB) because it was isolated from children with this syndrome. An outbreak of the disease occurred in north east Kent in the winter of 1958–59. Virus was isolated from 2 of 5 patients tested, and an antibody rise was detected in the serum of one of the 2 and also in one other patient. 2 of the 3 patients aged 7 months to 4 years in whom infection with parainfluenza 2 virus was proved were quite severely ill, but recovered. 1 fatal case is described though no laboratory studies were made. It is pointed out that other isolations of this virus have been made in the north of England by GARDNER *et al.* [this *Bulletin*, 1960, v. 35, 782] and that 33% of children under 8 years of age living in the Sheffield area have antibodies [CLARKE and SAYNOR, *ibid.*, 203].

D. A. J. Tyrrell

SMORODINTSEV, A. A. & SELIVANOV, A. A. **Results of Immunization of Volunteers with Live Attenuated Types IV, V and VII Adenovirus Vaccine.** (Preliminary Report.) *Problems of Virology*. London. 1959, v. 4, No. 6, 6–10. [Translated from Russian.]

"Reference strains" of adenoviruses types 4, 5 and 7 were passed 4 to 6 times in monkey kidney cells and gave fluids of titre 10^3 or 10^4 (volume and test cell not stated). 0·5 ml. of fluid of titre 10^3 was administered as a nasal spray to volunteers. The results were similar with vaccine of each serotype. Virus was recovered from the nasopharynx of 60 out of 66 volunteers, 12 of whom developed fever of 37·5°C. or over for 2 to 3 days. Nearly all of these volunteers showed rises of circulating antibody level as judged by neutralization

test (54) or complement-fixation test (56). These titres fell about 4-fold in 8 months after vaccination. Furthermore 9 volunteers who had been infected with type 5 virus were given 10 times more virus 5 months after the first administration, and suffered no symptoms. Virus was recovered from 1 volunteer on one occasion only after rechallenge, otherwise no virus could be recovered. [This paper is interesting and encouraging but it appears probable that the viruses used had been passed through HeLa cells. One would also like to know if a more dilute inoculum would have been effective.]

D. A. J. Tyrrell

MURRAY, H. G. S., FIELD, C. M. B. & MCLEOD, W. J. **Mumps Meningo-Encephalitis.** *Brit. Med. J.* 1960, June 18, 1850–53, 1 chart.

The clinical, laboratory, and epidemiological features of 50 cases of mumps meningo-encephalitis are described; 39 of the cases were seen during a mumps epidemic in Northern Ireland. In this setting an unusually large proportion of cases of meningo-encephalitis without salivary gland enlargement (46%) was suspected as being due to mumps, and confirmation was obtained by complement-fixation tests with V (viral) and S (soluble) antigens.

The principal clinical features were fever, headache, neck rigidity, and vomiting, with increased cells and protein in the spinal fluid; clinical encephalitic signs occurred in addition in about one-third of the patients. The peak incidence was in late spring and early summer. A follow-up study showed that 18% were still complaining of headache or "nervousness" when seen a year later [a not uncommon finding in a follow-up of any form of acute meningitis]. Sequelae were more common in the patients who had had encephalitic signs than in those who had had meningeal signs only. One child of 6 years died of the post infective type of encephalitis developing 3 weeks after the onset of mumps. The prognosis of mumps meningo-encephalitis, however, is usually good.

H. Stanley Banks

MATTMANN, E. & PULVER, W. Virologische und serologische Untersuchungen bei akuter Meningitis serosa. [**Virological and Serological Investigations in Acute Serous Meningitis**] *Schweiz. med. Woch.* 1960, June 11, v. 90, No. 24, 661–3. [25 refs.]

In the serological investigation of 170 patients suffering from serous meningitis observed in Lucerne in 1956–57 the diagnosis could be established in 78% of cases. There were 75 cases of poliomyelitis, 50 of which were paralytic, 12 of leptospirosis, 45 ECHO virus infections, and 1 case each of mumps and suspected Q fever. Attempts to isolate virus from the stool were carried out in 150 cases. From patients suffering from paralytic poliomyelitis 25 strains of type I, 2 of type II and 2 of type III poliomyelitis virus were isolated. In neutralization tests carried out on paired sera from patients suffering from virologically confirmed poliomyelitis a rise in homologous titre was found in only 17 of 40 (43%) instances, whereas the complement-fixation test gave positive results in 70%, of which only 30% were type-specific. An unspecific rise in titre of poliomyelitis complement-fixing antibody was found in 34% of 48 patients suffering from ECHO-4 and ECHO-9 meningitis. The authors conclude that virus isolation is more reliable than serological tests in the diagnosis of serous meningitis.

D. J. Bauer

GRIST, N. R., LARMINIE, H. E., MACGREGOR, L. G., MCINTOSH, E. G. S., MCLAUGHLIN, J. & SOMMERVILLE, R. G. **Poliomyelitis: a Laboratory Study during Two Seasons.** *Scottish Med. J.* Glasgow. 1960, Aug., v. 5, No. 8, 355–60. [14 refs.]

This interesting paper describes laboratory investigations of the majority of cases of suspected poliomyelitis occurring in south west Scotland in the period May 1956 to December 1957. Material from 465 patients was examined and the authors are confident that these included all the cases of poliomyelitis among the age-groups eligible for poliovaccine. It was found that HeLa, human and monkey kidney cells were of similar efficiency for the isolation of polioviruses but that HeLa cells were superior for adenoviruses, and monkey kidney cells for enteroviruses other than polio. Serological tests did not add very many extra aetiological diagnoses.

Poliovirus infection was demonstrated in 76% of the cases with paralytic poliomyelitis. 1 case was shown to be infected with Coxsackie A7 by isolation of the virus in suckling mice. 5 paralytic patients were infected with adenoviruses and 3 of these were also infected with polioviruses. The authors note that this illustrates the difficulty of ascribing a definite aetiological role to an infecting virus without ancillary evidence. An aetiological diagnosis was made in 45% of the cases of abacterial meningitis but poliovirus only accounted for 35% of the 108 diagnosed cases. 4 were Coxsackie A infections, 43 ECHO virus (mainly ECHO 9), 4 adenovirus and 6 unidentified. 1 of 16 patients with miscellaneous paralytic disease was infected with poliovirus type 1. In view of the findings of LIKAR and DANE [this *Bulletin*, 1958, v. 33, 558] that louping ill causes some paralytic disease in Northern Ireland, serological tests with this virus were made on 17 patients with paralysis or encephalitis but in none was a diagnostic titre or titre change observed.

A. J. Beale

GERFELDT, E. Vom Erscheinungswandel der Poliomyelitis. Zur Epidemiologie und Sozialpathologie der Poliomyelitis in Deutschland. [**The Changing Picture of Poliomyelitis. Epidemiology and Social Pathology of Poliomyelitis in Germany**] *Arch. f. Hyg. u. Bakt.* 1960, Aug., v. 144, No. 6, 442–51, 7 figs. [52 refs.]

This is a short but interesting paper in which the author describes and discusses, with particular reference to experience in Germany, the well-known changes in the picture of poliomyelitis which are compared with observations in other countries.

Sections of the paper deal with the (1) epidemiology

of poliomyelitis since before 1909 when the disease appeared to occur only occasionally, to the post-war years when large epidemics arose in many countries, (2) social pathological factors which influence the incidence, the changes in age distribution and in case mortality, and (3) the prophylaxis by generally accepted methods and by specific immunization.

The opinion is expressed that prophylactic measures and in particular immunization procedures will not be really effective until they are carried out on an international basis. *M. E. Delafield*

TERNI, M., POLI, L. & TANGHERONI, W. Considerazioni su due episodi di poliomielite in collettività infantili. **[Considerations of Two Incidents of Poliomyelitis in Child Communities]** *Giorn. di Malattie Infettive e Parassit.* 1960, May–June, v. 12, Nos. 5/6, 232–43, 3 figs. [39 refs.]

Both outbreaks occurred in institutions in Pisa and the authors have studied and typed the virus isolated from the faeces of those involved, including certain contacts.

One outbreak was in the isolation ward of the Paediatric Clinic and the investigation covered the period of January–June 1957. The 10 children who occupied the isolation ward at the time had been admitted for acute bronchitis (6), influenza (2) and whooping cough (2) and had all had treatment with penicillin and streptomycin intramuscularly. None had received any poliovaccine. Following the appearance of the first case of poliomyelitis in this group, 6 of the other children were given gamma globulin by way of prophylaxis which did not prevent 2 of these developing a paralytic infection. There were 5 cases in all, the respective onsets being on January 24, February 2, 3 and 11 and March 18: each developed a paralysis of the lower limbs. A type 1 virus was isolated from the faeces of 8 out of these 10 children, 4 of the 8 showing no clinical disease.

The authors report the laboratory technique which they have followed.

The other episode was investigated in a Foundlings' Home during July 1956–July 1958. A type 2 virus was isolated from 13 out of 49 child inmates (26%) but only one child became ill at the time, with paralysis. Later, ECHO 8 virus was found to be circulating widely in this community without giving rise to any clinical manifestations. 10 months later there appeared a second case of poliomyelitis, also paralytic and type 2.

The authors discuss the meaning of the ratio between paralysis and total infection in the 2 episodes and they try to explain the reason why ECHO 8 virus followed the poliovirus. *J. Cauchi*

BONDARENKO, O. M. **Data on Poliomyelitis in the Armenian S.S.R.** *Problems of Virology.* London. 1959, v. 4, No. 5, 39–42. [Translated from Russian.]

"(1) Beginning from 1950 cases of paralytic poliomyelitis were registered annually in the Armenian S.S.R. in towns as well as in some of the country districts and republics. The highest morbidity in the republic was observed in 1955 (37 cases) and in 1957 (40 cases) and an increase in the morbidity could also be seen in 1958 (49 cases within the first 9 months of the year).

"(2) In the Armenian S.S.R. poliomyelitis mainly affects children under 7 (95·9 per cent of all cases) and particularly children between 1 and 2 years of age (54·2 per cent).

"The highest number of cases occurs in the summer and autumn months.

"The morbidity was of widely scattered character; epidemiological investigation of foci of infection rarely revealed the source of infection.

"(3) Virological investigations of material collected from patients and from persons who had been in contact with patients by means of tissue culture revealed that types I and III virus were circulating and that type I virus predominated.

"(4) Preliminary studies regarding the immunological structure in the child population in regard to poliomyelitis revealed that in 73·8 per cent of children over 4 years antibodies to various types of poliomyelitis virus could be found. Among younger children this percentage was considerably lower (50·2 per cent). Antibodies to all three types of virus were found in only 12 per cent of all healthy children under 8 years."

LÉPINE, P. Sur l'antigénicité des vaccins contre la poliomyélite. Vaccins inactivés et vaccinations par virus vivants atténués. **[Antigenicity of Poliomyelitis Vaccines. Inactivated Vaccines and Vaccination with Attenuated Living Viruses]** *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 23/24, 480–98. [64 refs.]

This is a long summary of the present position of poliomyelitis prophylaxis. Killed poliovaccine has been proved safe and effective but it has drawbacks, in particular that it only protects the individual, not the community. Attenuated poliovaccines have been less thoroughly tested. There is little information about efficacy but safety of Sabin's strains in Russia seems indubitable. The Sabin strains are the most attenuated for monkeys. The problems of genetic stability, interfering viruses and control of manufacture are all vexing and difficult. Lépine concludes that the 2 sorts of poliovaccine are not mutually exclusive. For mass campaigns in developing countries one method may be applicable, for individual protection the other. *A. J. Beale*

SPIGLAND, Ilya & GOLDBLUM, N. **Immunization of Infants with Formalinized Poliomyelitis Vaccine (Salk Type).** *Pediatrics.* Springfield, Ill. 1960, May, v. 25, No. 5, Pt. 1, 812–21, 6 figs. [18 refs.]

Immunization against poliomyelitis should take place in early infancy since, in many parts of the world, the main brunt of the incidence falls on infants. The effectiveness of killed poliovaccine in producing antibodies was investigated in Israel by using locally made, highly potent poliovaccine having an antigen extinction titre in guinea pigs of about $10^{-3.0}$ for types 1 and 2 and rather lower for type 3. Maternal antibodies were

present in the vast majority of infants at birth—94%, 94% and 87% for types 1, 2 and 3, respectively—but at 5 or 6 months the percentages had fallen to 15, 16 and 11. By giving 2 inoculations 1 month apart it was found that the older the infants were at the first inoculation the better the response. Thus, for type 1, 39%, 58% and 80% responded at 1, 3 and 5 months. The responses were better for type 2 and rather worse for type 3. 3 inoculations gave better responses than 2 in infants of 5 months of age. Thus, for type 3, 53% responded with 2 doses and 85% with 3 doses. It seems likely that maternal antibodies rather than young age is the most important factor in the failure to respond to infection. This conclusion is not certain since it is the young children in general who have high maternal antibody levels. When booster doses were administered it was found that the children who were given their primary doses at 1 or 3 months and failed to respond developed antibodies. Thus, in 35 children, 32 had no antibodies after a primary course and none had them before the booster dose. After the booster dose, 33 developed antibodies, 23 having titres of 1 in 32 or higher. The response to type 2 was better but type 3 was worse.

The authors conclude that for maximal primary responses poliovaccination should be delayed until 5 or 6 months. However, perfectly satisfactory immunization can be achieved after the booster dose in children first vaccinated at 1–4 months. The authors stress the importance of employing highly potent vaccine for primary immunization.

[See also this *Bulletin,* 1960, v. 35, 56.] *A. J. Beale*

QUAADE, F. **The Influence of Salk's Vaccine on the Course of Acute Anterior Poliomyelitis.** *Acta Med. Scandinavica.* 1960, Aug. 31, v. 167, No. 6, 427–30.

A study of the severity of poliomyelitis in vaccinated and unvaccinated patients admitted to hospital in Copenhagen in the years 1956–58 is presented. There were 68 patients, 49 vaccinated with 2 or 3 doses intracutaneously and 19 unvaccinated (2 had had 1 dose of vaccine). The severity was less in the vaccinated; their average stay in hospital was 39 days compared to 62 days. 22% of vaccinated cases were non-paralytic against 11% in the unvaccinated. Bulbar or extensive paralysis occurred in 73% of unvaccinated and 39% of vaccinated cases. The poliovirus type isolated was given for 43 out of 49 vaccinated and 18 out of 19 unvaccinated cases. It is not stated if virological confirmation was achieved in the other 7 cases.

[BROWN *et al.* (this *Bulletin,* 1960, v 35, 677) have also reported that poliomyelitis may be less severe in the vaccinated.] *A. J. Beale*

EICHENWALD, H. F. & KOTSEVALOV, Olga. **Immunologic Responses of Premature and Full-Term Infants to Infection with Certain Viruses.** *Pediatrics.* Springfield, Ill. 1960, May, v. 25, No. 5, Pt. 1, 829–39, 1 fig. [15 refs.]

It is commonly supposed that the immunological response of newborn infants is poor. During a 5-year study of virus infections in newborn and premature infants examples of infection with ECHO 9, 18, and 20 and adenovirus 1, 2, and 3 were studied. It was found that the antibody response of newborn children was quite good and varied more with the type of virus than with the age of the host. In 5 infants who became infected with viruses 4 were actively immunized despite the presence of passive maternal antibodies. However, the frequency with which passive antibodies may have prevented infection in unknown. Good antibody responses occurred after ECHO 9, 18 and 20 infection and did not seem to depend upon whether a clinical illness was produced. An antibody response to adenovirus infection was less uniform. Thus, 3 out of 11 subjects infected with types 1 or 3 adenovirus failed to develop antibodies. *A. J. Beale*

PAGANO, J. S., PLOTKIN, S. A. & KOPROWSKI, H. **Variation of Response in Early Life to Vaccination with Living Attenuated Poliovirus and Lack of Immunologic Tolerance.** *Lancet.* 1960, June 4, 1224–6. [Refs. in footnotes.]

Attenuated poliovaccine (CHAT type 1, P-712 type 2 and W-Fox type 3) was administered to 47 premature infants (type 1 only) and 149 full-term infants. The full-term infants received vaccine between term and 180 days. It was found that 94% of the premature infants became infected but only 56% of those infected developed antibodies. Term infants under 5 days old showed a similar pattern. Infants from 5 to 60 days old were less commonly infected (about 75%) but if infected usually (about 90%) developed antibodies. By contrast, infants over 60 days were usually successfully infected (89%) and 96% of those infected developed antibodies. Failure of premature or term infants to make an antibody response despite multiplication of virus in their intestinal tracts did not impair their ability to respond to vaccine virus administered when they were older. There was thus no evidence of immune tolerance to poliovirus.

[There is evidence that newborn infants can make a satisfactory immune response to some viruses (see above). See also this *Bulletin,* 1959, v. 34, 1087.]

A. J. Beale

LÉPINE, P., SAMAILLE, J., MAURIN, J., DUBOIS, O. & CARRÉ, M. C. Isolement du virus ECHO 14 au cours d'une épidémie de crèche de gastro-entérites. **[Isolation of ECHO Virus Type 14 during a Gastro-Enteritis Epidemic in a Public Nursery]** *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 161–6.

ECHO 14 virus was isolated from 3 babies (9, 14 and 16 months) in a nursery in which there was an outbreak of severe gastro-enteritis. The same virus was isolated from 10 out of 20 babies in contact who were examined. 2 were excreting poliovirus type 3. 2 of the 3 patients showed a rise in titre of neutralizing antibodies to ECHO 14 during convalescence but 1 had no antibodies

at a dilution of 1/10. 7 babies excreting ECHO 14 and 2 babies from whom the virus was not isolated had antibodies to ECHO 14 in sera taken after the epidemic.
A. J. Beale

STEIGMAN, A. J. & LIPTON, M. M. **Fatal Bulbospinal Paralytic Poliomyelitis due to ECHO 11 Virus.** *J. Amer. Med. Ass.* 1960, Sept. 10, v. 174, No. 2, 178–9.

"A 2-year-old child with fatal bulbospinal paralytic poliomyelitis was infected with an ECHO 11 virus to which she developed antibody. At no time was poliovirus antibody detected in any of her serial blood serums. Awareness of the danger that nonpolio enteroviruses can cause poliomyelitis disease and fatalities is emerging. The frequency with which this may happen is as yet undetermined and merits continued close surveillance and concern in its own right and in evaluation of poliovaccine failures."

BOS, G. J. De epidemie van hepatitis infectiosa gedurende 1958–1959 en het gebruik van gammaglobuline hierbij in de huisartsenpraktijk. [**The 1958–1959 Epidemic of Infective Hepatitis and the Administration of Gammaglobulin in General Practice**] *Nederl. Tijdschr. v. Geneesk.* 1960, July 2, v. 104, No. 27, 1278–83, 3 figs. English summary.

In July, 1958, the author observed a case of infective hepatitis in a 5-year-old boy in Vlaardingen, Holland, which was followed by 4 successive cases in the same family in the following 3 months. In the 12-month period ending in July 1959 he further observed 65 cases of the disease among 39 families with 243 members, who formed part of his practice in the same town; 5 patients had previously suffered from infective hepatitis in 1953–54, and it is suggested that their lack of immunity might be due to the existence of more than one type of infective hepatitis virus. The disease was 2½ times more frequent in sickness insurance patients than in private patients, and the mean ages of these 2 groups of patients were 8·6 and 16·3 years respectively. Gamma globulin was administered prophylactically in a dose of 0·02 ml. per kgm. to 58 children who were in contact with the infection, 1 of whom subsequently developed the disease in an anicteric form; 1 case also occurred among 21 children who were given gamma globulin in a dose of 0·01 ml. per kgm., whereas in a control group of 123 exposed persons aged up to 40 years or more, 24 cases occurred. Finally, in a summary of the advantages of using gamma globulin in the prophylaxis of infective hepatitis in general practice, attention is drawn to the fact that gamma globulin prepared in Holland is about one-quarter of the price of that obtained from America. *D. J. Bauer*

LEVINE, R. A. & PAYNE, Mary A. **Homologous Serum Hepatitis in Youthful Heroin Users.** *Ann. Intern. Med.* 1960, July, v. 53, No. 1, 164–78, 6 figs. [21 refs.]

Of 21 youthful narcotic users 13 gave histories of 1 or more attacks of jaundice: biochemical evidence of hepatic dysfunction was present in 14, while only 4 gave clinical symptoms or signs of liver disease. The level of serum glutamic oxalacetic transaminase proved useful in the detection of subclinical liver damage. The most likely cause of persistent hepatic dysfunction in the group seemed to be repeated infection by unsterilized needles. *A. B. Christie*

LVOV, D. K. [**Immunological Pattern of the Population in the Birilyussk District of the Krasnoyarsk Region with respect to Tick-Borne Encephalitis**] *Med. Parasit. & Parasitic Dis.* Moscow. 1960, v. 29, No. 4, 398–405. [17 refs.] [In Russian.]

The English summary appended to the paper is as follows:—

"An immuno-epidemiological examination of the rural population was effected during 1958–1959 for tick-borne encephalitis in settlements belonging to the southern sub-zone of the taiga belt. Altogether 492 sera were examined in complement fixation tests and 369—in neutralization reactions. Complement-fixing antibodies were revealed in 25–30% of persons, their presence in children aged up to 5 years being encountered twice less frequent. In children aged up to 7 years the virus-neutralizing antibodies were disclosed in 21% of those examined, in those of the 8–15 years—in 65% and among adults in 90–100% of cases. The principal anti-epidemic measure in residential areas, similar to the ones described, should be specific prophylaxis with the institution of a complete vaccination course among the newcomers and children of pre-school and school age. There were registered from 9 to 30 instances with inapparent course of the affection for each clinically certified case of tick-borne encephalitis."

SOBĚSLAVSKÝ, O., REHN, F. & FISCHER, J. Izolace viru klíštové encefalitidy z lysky černé (*fulica atra*). [**Isolation of Tick-Borne Encephalitis Virus from the Moorhen (*Fulica atra*)**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 4, 256–61, 1 graph. [17 refs.] English summary.

During the course of an investigation of the distribution of ornithosis virus among wild birds [the locality in Czechoslovakia is not stated] the authors isolated a strain of virus which was identified as tick-borne encephalitis virus by cross-neutralization and fixation tests with reference materials. The virus was isolated from the brain and spleen of 1 of 30 moorhens (*Fulica atra*) by the intracerebral inoculation of mice, and grew well in cultures of HeLa and chick embryo fibroblast cells. It was not possible to establish whether the moorhen is a natural reservoir of the virus.
D. J. Bauer

BÁRDOS, V. Sérologicko-epidemiologická metóda štúdia charakteristiky arbor-vírusu Tahyna a jeho ekológie. **[The Serological and Epidemiological Method of studying the Characteristics of the "Tahyna" Arbor Virus and its Ecology]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, Nos. 5/6, 361–3.

The author has investigated the incidence of neutralizing antibody in the population of Slovakia to the Tahyna strain of arborvirus [this *Bulletin,* 1960, v. 35, 207]. The neutralization test was carried out in mice with undiluted serum and 100 LD50 of virus. Positive results were obtained in 30 of 99 (30·3%) inhabitants of an area badly affected by mosquitoes, in 23 of 175 (13·1%) in a less severely affected area, and in 6 of 245 (2·4%) in a relatively unaffected area, and also with the sera of 35 of 102 horses, 7 of 88 donkeys and 4 of 156 cows. *D. J. Bauer*

ASHLEY-MILLER, M. & FANNING, D. M. **Measles in General Practice, January–April 1959.** *Practitioner.* 1960, June, v. 184, No. 1104, 781–7.

The setting of this measles outbreak was an isolated Royal Air Force Station comprising 3 separate housing sites of 168 houses in all, and 4 caravan sites totalling 40 caravans. There were 372 children, 224 of whom had never had measles previously and of these 52·7% developed the disease. The infection appeared to be spread and maintained chiefly through the schools; among 29 susceptible children who lived in caravans and did not go to school, only 2 developed the disease.

Gamma globulin was unsuccessful as a prophylactic because it was given too late in the incubation period, or in insufficient dosage. Clinically the dry barking cough was the most characteristic sign in the prodromal period. Secondary infection of chest, throat, and ears occurred in 35·5% of those affected, and was satisfactorily treated by prompt oral penicillin. [It is worthy of note that in this epidemic about half of the susceptibles escaped the disease.] *H. Stanley Banks*

SMORODINTSEV, A. A., BOICHUK, L. M., SHIKINA, E. S., BATANOVA, T. B., BYSTRYAKOVA, L. V. & PERADZE, T. V. **Clinical and Immunological Response to Live Tissue Culture Vaccine against Measles.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 201–14. [10 refs.]

The authors report the results of a clinical investigation of a live measles virus vaccine, which has previously been described in the Russian literature. The vaccine was prepared from the Leningrad 4 strain of attenuated measles virus grown in chick embryo fibroblast or human amnion cell cultures. Of 113 susceptible children aged 2–6 years vaccinated intradermally or subcutaneously with 25–100 TCD50 of the virus, 87 developed an illness resembling an abortive attack of measles. 69 of 85 developed a rise in antibody titre, and in 41 of 92 the virus could be recovered from the blood or respiratory tract. No signs of measles infection could be observed in 148 children who were in close contact with the vaccinated children. No evidence of take could be obtained in 32 children who received the vaccine epidermally or by nasal spray. A detailed analysis of the clinical manifestations and the serological response to vaccination is presented. Immunity only developed in those children who developed a mild illness resembling measles, and the authors draw attention to the parallel in this respect with smallpox vaccination. The illness was benign in all cases, and the vaccine was considered to be fully acceptable for large-scale use. *D. J. Bauer*

CHANG, C. T. **On the Use of Arakawa Vaccine in the Prevention of Measles.** *Yokohama Med. Bull.* 1960, Feb., v. 11, No. 1, 21–32, 6 figs. [17 refs.]

The author has carried out clinical trials of a measles vaccine developed by ARAKAWA [this *Bulletin,* 1954, v. 29, 1134], consisting of suspension of chick embryos infected with a number of Japanese strains of measles virus. The vaccine was injected subcutaneously in 3 doses at intervals of 1 week; the first dose of vaccine had been inactivated with sodium mercurithiosalicylate, and the other 2 contained live virus. In 1955, 29 susceptible children aged 6 months to 7 years were vaccinated in a kindergarten in Tokyo; during an epidemic of measles which began 1 month after the end of vaccination 5 (17%) developed a mild attack of the disease. In similar circumstances in 1957 15 of 67 (22%) vaccinated children developed the disease. In 1959 109 susceptible children aged 6 months to 7 years living in a residential area in Tatebayashi were treated with the vaccine; during a subsequent epidemic 65 (60%) developed measles, mostly of mild character, compared with 156 of 164 (95%) children in an unvaccinated control group. *D. J. Bauer*

KEITH, T. A. **Periodicity of Mononucleosis-Like Disease at an Army Post.** *Amer. J. Med. Sci.* 1960, Sept., v. 240, No. 3, 340–45. [29 refs.]

With restricted laboratory facilities, the author based diagnosis of infectious mononucleosis on suggestive clinical signs coupled with an unabsorbed sheep cell agglutinating titre of 1 in 112 in the patient's serum. During 1957, of 191 sera examined, only 14 gave this titre (7·33%), but in 1958 of 274 examined 99 were positive (36·3%). Of 99 cases, 66 occurred during the 4 months February to May. The author considers that the difference between the incidence in the 2 years and the concentration on the 4 months in 1959 can be explained only by the periodicity of the disease, as other factors were stable for the 2 years.
A. B. Christie

EVANS, A. S. **Infectious Mononucleosis in University of Wisconsin Students. Report of a Five-Year Investigation.** *Amer. J. Hyg.* 1960, May, v. 71, No. 3, 342–62, 8 figs. [34 refs.]

This is an important complehensive study of the aetiology, pathogenesis, and clinical aspects of infectious

mononucleosis from a well-known student of the subject. The disease seems to have a particularly high incidence in American college students—the basis of the author's material. It represents 12 to 35% of hospital admissions for respiratory-like illnesses University of Wisconsin students and 3·5 to 7·5% of total admissions.

Like other investigators, the author failed to isolate a causative virus, although he tried various types of tissue culture with material from 152 patients. Again, like other investigators, he found that apparent transmission of the illness from one person to another under natural circumstances was infrequent, but when it did occur, intimate oral contact (kissing) was a frequent though not exclusive feature [HOAGLAND, this *Bulletin*, 1955, v. 30, 740]. Heterophile-positive and heterophile-negative cases seem to represent the same disease clinically, and often haematologically, and this serological aspect is considered to be merely a matter of differing quantitative responses of the host to the same causative agent. The presence of heterophile antibody represents greater severity, and is often accompanied by longer duration of illness, greater aberration of liver function tests, and an appreciably higher lymphocytic count.

A new concept of pathogenesis is suggested. The disease may exist in three phases, the first two of which may often escape diagnosis. Phase I is the primary abortive phase, characteristically seen in childhood, with a short incubation period and mild fever without specific features, often of epidemic distribution; in this phase the causative virus may be limited to local sites in the body. Material for diagnosis should be collected in this phase if it can be recognized. Phase II is the intermediate viraemic phase, with fever, early adenopathy, frequent rash, mild or moderate lymphocytosis, but antibody not yet detectable or in low titre. The relatively high incidence of a rash in heterophile-negative cases would be in keeping with this concept. Phase III is that of tissue reaction to virus multiplication in secondary sites, for example lymph nodes, liver, and spleen; there is an absolute lymphocytosis, and well-marked heterophile antibody, making the disease easily recognizable. This is the characteristic manifestation in the young adult, and the absence of recognition of the earlier phases suggests the *apparently* long incubation period. Phase III is of low infectivity, and transmission may require high dosage of the infective agent. It is affirmed that this concept was inherent in Pfeiffer's original description of the disease in 1889, but proof could be obtained only by isolation of the causative virus. *H. Stanley Banks*

LYMBURNER, R. M. & MALCOLMSON, C. H. **Thrombocytopenic Purpura complicating Infectious Mononucleosis.** *Canadian Med. Ass. J.* 1960, Sept. 17, v. 83, No. 12, 652.

Report of a case.

HUGHES, J. P. & PAULLEY, J. W. **Steroid Therapy in Glandular Fever.** *Postgraduate Med. J.* 1960, Sept., v. 36, No. 419, 553–6.

The authors give clinical details of 10 patients suffering from glandular fever, all fairly severely ill and all treated with corticosteroids, usually prednisone in a dose of from 20–60 mgm. daily. They list 5 clear-cut indications for such therapy—hepatic complications, some anginose states, encephalitis, polyneuritis and thrombocytopenia—but they feel that there is no point in withholding steroid therapy in any severe case of glandular fever whether complicated or not. [The case reports require careful study. The least impressive one relates to a patient not admitted to hospital and not apparently a severe case: "There was a marked clinical improvement in seven days . . . progress was maintained whilst steroids were tailed off during the next seven weeks". In other cases improvement was dramatic.] *A. B. Christie*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

MUROHASHI, T. & YOSHIDA, K. **Biological Meaning of the Differential Stainability of *E. coli* to Malachitegreen-Fuchsin Staining.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 369–80, 6 figs.

"Malachite-green-fuchsin staining was demonstrated on Gram-negative bacteria, *E. coli*, a representative of this bacterial group, and quite similar results were obtained in the differential staining as well as in the correlation between the viability and the differential stainability just as in Mycobacteria. Accordingly, it was assumed that living cells stain green, while pink stained cells were the dead.

"Pretreatment with tannic acid, in order to obtain

differential staining of the cells, is very interesting in suggesting the differences of the cell wall structures among various bacterial groups."

MUROHASHI, T. & YOSHIDA, K. **Biological Meaning of the Differential Stainability of *Staphylococcus aureus* to the Malachite-Green-Fuchsin Staining.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 467–79, 6 figs.

"Malachite-green-fuchsin staining was used on *Staphylococcus aureus*, a representative of Gram-positive bacteria, and quite similar results were observed as in Mycobacteria and Gram-negative bacteria. A very close relationship was shown between the differential stainability and the viability of bacterial cells. The differential stainability by the authors' procedure is completely independent of the Gram's method, and the hydrolysis of RNA-compound with ribonuclease did not affect even the stainability to malachite-green as well as to the viability of the bacterial cells. The decrease in the stainability using Gram's method in the course of preservation was obviously slower than that to malachite-green.

"From the results and the results obtained on Mycobacteria and *E. coli*, it seems most likely that the authors' malachite-green-fuchsin staining method presents biological significance from the stand point of differential staining the living from the dead bacterial cells. Because the staining procedures to achieve similar staining effects are slightly different, depending on the bacterial species used, this may suggest differences in their cell wall structures to some extent."

AUSTRIAN, R. **The Gram Stain and the Etiology of Lobar Pneumonia, an Historical Note.** *Bact. Reviews.* 1960, Sept., v. 24, No. 3, 261–5. [18 refs.]

MACCACARO, G. A. & DETTORI, R. **Studies on Bacterial Fimbriae. VI. Agglutination of Fimbriated Cells by Dipolar Molecules.** *Giorn. di Microbiol.* Naples. 1960, Apr.–June, v. 8, No. 2, 65–82, 4 figs. [15 refs.]

ISEKI, S., SAEKI, N. & FURUKAWA, K. **Immunochemical Studies on Bacterial Blood Group Substances. I. Absorption of the Blood Group Specific Antibodies in Bacterial Antisera by Simple Sugars.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 455–9. [17 refs.] **II. Sugar Composition of Bacteria containing Blood Group Substances.** *Ibid.*, 461–6. [21 refs.]

DEL VECCHIO, V. & D'ARCA SIMONETTI, A. Modifica pratica del metodo di Bray e King per la ricerca della fosfatasi microbica. [**A Modification of the Bray and King Method for Detection of Bacterial Phosphate**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Mar.–Apr., v. 11, No. 2, 133–40.

The English summary appended to the paper is as follows:—

"The authors suggest the replacement of the Dorset culture medium with the agar-milk medium in the performance of Bray and King's method.

"The proposed medium is very simple, and consists of a 6% aqueous suspension of agar added to an equal volume of skimmed milk.

"The new medium combines the advantages of the Dorset medium with those of scarce susceptibility to proteolytic enzymes, and high sensitivity to even small amounts of phosphatase and is extremely simple to prepare."

[See this *Bulletin*, 1944, v. 19, 58.]

FIKHMAN, B. A. **A Microrefractometric Method for Direct Determination of Live and Dead Bacterial Cells.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 8, 121–5, 3 figs. [Translated from Russian.]

This is an interesting and well-written paper which shows how the alteration in the refractive index of a bacterial cell when it dies can be exploited to yield a practical method for the visual determination of the living or dead state of the cells in a bacterial suspension. It is a development of a method introduced by BARER and ROSS (*J. Physiol.*, 1952, v. 118, 38*P*) for the microscopic refractometry of the living cell with the aid of phase-contrast apparatus and protein immersion media.

Clarified and purified gelatin gels prepared in distilled water provide immersion media having a refractive index almost exactly equal to the refractive index of the cytoplasm of the living bacterial cell. Viewed through a phase-constrast microscope a suitably mounted bacterial suspension in this immersion medium shows the living cells as "hollows", each bordered by a thin ring—the cell wall. That is to say, the cytoplasm is not visible because it has the same refractive index as the immersion medium and only the cell wall can be defined. The dead bacterium has a different refractive index from the immersion medium and is therefore seen as a solid object; finer differences may be observed with suspensions of killed bacteria, depending on the method of killing. Organisms killed by heat or alcohol appear as solid objects shining more brightly than those killed by phenol or merthiolate. On the other side, very young living cells have a lower refractive index than other living cells in the population so that the "hollow" inside the thin ring of the cell wall may appear darker than the background.

While it is a little uncertain how far these observations may be applied in practice, they are of very considerable interest. *H. J. Bensted*

RUBBO, S. D., PRESSLEY, T. A., STRATFORD, B. C. & DIXSON, Shirley. **Vehicles of Transmission of Airborne Bacteria in Hospital Wards.** *Lancet.* 1960, Aug. 20, 397–400, 2 figs. [10 refs.]

Bacteria and dust in the air of 3 hospital wards were collected on settling plates held at 0, 3, 6 and 9 ft. above the floor. The dust was collected on gelatin plates from which it was later recovered for identification of the fibres by staining [this *Bulletin*, 1959, v. 34, 149]. The

total bacteria and staphylococcus counts were very similar at all levels. The fibre count at floor level averaged 0·074 mgm. per 24 hours per 9 cm. Petri dish; at 6 and 9 ft. it was 0·004. The proportion of the fibres staining as cellulose was 79% at floor level and 93% at 9 ft.; the balance stained as protein. These results support the view that the bacteria are present in the air either free or associated with microscopic fibre particles referred to as fibre nuclei. *R. E. O. Williams*

RUBBO, S. D. & DIXON, Shirley. **A Contact-Plate Technique for determining Bacterial Contamination of Fabrics.** *Lancet.* 1960, Aug. 20, 394–7, 5 figs.

2 methods are described for determining the bacterial flora of blankets and similar fabrics. In 1 the fabric is stretched over an aluminium disc in such a way that a culture plate can be brought into contact with it. In the 2nd the fabric is held stretched about 5 cm. above a culture plate, and a 250 gm. steel ball is dropped on to it from a height of 40 cm., after which ½–1 minute settling is allowed. The number of percussions could be varied. These 2 methods were compared with the sweep plate [number of sweeps not stated]; both had the advantage of giving a more even distribution of colonies over the plate. The contact plate and the sweep plate gave similar numbers of colonies. With unoiled blankets the number of colonies obtained by percussion was larger; with oiled blankets it was less than with the other 2 methods. With the sweep plate the sharpness of the edge of the dish was found to be important. The contact plate technique is simple, rapid and economical and can be used for all types of textiles. [There is no discussion of the variation in count to be found in different areas of the same blanket; it seems likely that this may often be great enough to make an attempt at a precise count somewhat hazardous.] *R. E. O. Williams*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection.**

GRÄF, W. & BICKEL, H. Antibiotische Beziehungen zwischen Algen und Bakterien. [**Antibiotic Relationships between Algae and Bacteria**] *Arch. f. Hyg. u. Bakt.* 1960, July, v. 144, No. 5, 421–9, 4 figs.

This paper is on a refreshingly unusual subject and reaches an unexpected conclusion. Algae are credited with some part in the self-purification of water, and have been shown to form at least one antibiotic (chlorellin). These authors hoped to show that algae exert some antibacterial effect *in vitro*, and obtained pure cultures of 3, which grew on solid media suitably illuminated. When various bacteria were streaked up to a streak of growth of an alga there was no sign of any growth inhibition.

They then decided to do the experiment the other way round, and found that previous growths of certain bacteria produce zones of inhibition of growth of some algae. *Staphylococcus aureus* and *Pseudomonas pyocyanea* inhibited both *Chlorella vulgaris* and *Nitzschia palea*: *Escherichia coli* and *Bacillus subtilis* inhibited only the former and *Pseudomonas fluorescens* only the latter. The blue alga *Oscillaria formosa* was unaffected by any of the bacteria. The inhibition observed (and illustrated) is said not to be an effect of change in *p*H or exhaustion of nutriment: that it is due to an antibiotic was proved in one instance by a test with the "pure" antibiotic substance extracted from *Ps. fluorescens*.

An antibacterial action supposed by a previous worker to be exerted by *Nitzschia palea* on *E. coli* is shown to be explicable by the combined action of the light necessary for algal growth and a silicate in the medium used. *L. P. Garrod*

LEADERS, F., PITTINGER, C. B. & LONG, J. P. **Some Pharmacological Properties of Selected Antibiotics.** *Antibiotics & Chemotherapy.* New York. 1960, Aug., v. 10, No. 8, 503–7, 2 figs.

These authors administered streptomycin, dihydrostreptomycin, chloramphenicol, tetracycline and oleandomycin intravenously to rabbits anaesthetized with phenobarbital sodium or urethane, and observed falls in blood pressure and electrocardiographic changes. In isolated organ preparations they also showed reduced contractility of the heart and of smooth muscle (ileum): there was also interference with the cat nictitating membrane. It is suggested that such actions as these may explain "undesirable cardiovascular effects associated with antibiotic therapy".

[Effects of this kind are very uncommon, and the doses used in these experiments are very large: those required to halve the blood pressure varied from 52 mgm./kgm. for streptomycin to 344 mgm./kgm. for tetracycline. Even the smaller of these doses, given intravenously, would produce a blood concentration far higher than any attained therapeutically.]

L. P. Garrod

GILLISEN, G. & STORBECK, W. Beeinflussung der Chemoresistenz von Mikroorganismen. [**Changing the Chemoresistance of Micro-organisms**] *Ztschr. f. Hyg. Infektionskr.* 1960, v. 146, No. 6, 552–62, 4 figs. [28 refs.]

Under this broad title the authors report observations on a narrowly restricted subject; this is the effect of the presence of 8-chlortheophyllin on the antibacterial activity of penicillin and some other antibiotics. This substance is said to enter into some kind of combination with penicillin [whether it does so with other antibiotics is unexplained], conferring on it greater stability and diffusibility. In the presence of a constant amount of 8-chlortheophyllin (4 mgm./ml.) the amount of penicillin required to inhibit the growth of resistant staphylococci, *Escherichia coli* and *Salmonella typhi* was less than in control cultures (but with differences of often only 2-fold): in further tests with streptomycin, chlortetracycline, bacitracin, etc., and including some bacterial species other than those mentioned, some further examples of a similar effect were observed, but the action of some drugs on some species was unaffected. Measurements of oxygen uptake also showed that 8-chlortheophyllin potentiated the action of penicillin on staphylococci: other experiments are described which showed that it diminishes both the growth rate and the mutation rate of these organisms. *L. P. Garrod*

PRIEST, Jean H., SIMON, A. J. & LEPPER, M. H. **Aerobic Bacterial Flora of the Throat of Children given Prophylactic Antibiotics. The Influence of Penicillin and Tetracycline on the Occurrence of *Micrococcus pyogenes* var. *aureus*; *Streptococcus pyogenes*, *Diplococcus pneumoniae*, and *Hemophilus influenzae*.** *Amer. J. Dis. Children.* 1960, July, v. 100, No. 1, 74–84. [15 refs.]

This study was carried out in a convalescent home for rheumatic children, among whom groups were given oral penicillin or tetracycline, or no medication for periods of 3–4 months. Swabs were taken at intervals from the nose, throat and naso-pharynx and examined for the presence of 4 species of bacteria. Coagulase-positive staphylococci (looked for in the nose only) usually antibiotic-resistant, were found in about three-quarters of the patients in all groups: there was little evidence of increase in resistance to the antibiotics administered. Haemolytic streptococci of Group A were found in only 1 patient. Pneumococci were found in 6% of cultures from controls, 4% of those taking penicillin and none of those taking tetracycline. *Haemophilus influenzae* was found in 21% of cultures from controls, about 45% of those taking penicillin, and only 3% of those taking tetracycline. *L. P. Garrod*

HANCOCK, R. **Streptomycin-Induced Lysis of Penicillin-Treated Staphylococci.** [Correspondence.] *Nature.* 1960, May 21, v. 186, 658–9, 2 figs.

Multiplying *Escherichia coli* is rapidly lysed by lethal concentrations of penicillin: *Staphylococcus aureus* is not. But it is here reported that minimal bactericidal concentrations of penicillin and streptomycin acting together (or when the streptomycin is added up to 50 minutes after the penicillin) cause rapid lysis of the latter organism. The effect is reduced by diminishing the peptone content of the medium, and almost abolished by the presence of chloramphenicol or of 8-azaguanine. *L. P. Garrod*

YONEDA, M., FUKUI, Y. & HORI, M. **Studies on the Mode of Action of Antibiotics. I. Quantitative Effect of Streptomycin on the Exponential Growth of a Strain of *Escherichia coli*.** *Biken's J.* Osaka. 1958, Nov., v. 1, No. 1, 61–9, 5 figs. [11 refs.]

These experiments were made with a strain of *Escherichia coli* for which the minimum inhibitory concentration of streptomycin was 6 μgm./ml. When lower concentrations than this (1 or 2 μgm./ml.) were added to cultures in the exponential phase of growth, the growth ceased for a short time but was then resumed at the same rate as in the control. The authors determined the influence on this effect of antibiotic concentration, time and temperature of pre-incubation, inoculum size and *p*H of the medium, and submit their results to elaborate mathematical analysis. One by-product of these studies is that since there is a linear relation between the streptomycin concentration and the logarithm of growth increment in a given short time such as 1 hour, this can be used as the basis of a simple rapid streptomycin assay method. *L. P. Garrod*

WEINER, L. M. & SWANSON, R. E. **Chloramphenicol-Resistant Strains of *Salmonella typhosa*. I. Induction of Morphological, Cultural, and Antigenic Changes.** *J. Bacteriology.* 1960, June, v. 79, No. 6, 863–8, 2 figs. [18 refs.]

A strain of *Salmonella typhi* susceptible to 0·7 μgm./ml. of chloramphenicol was trained to resist 20 and 200 μgm./ml. This change was accompanied by pleomorphism, a slower growth rate, and loss of motility. Serological studies, apart from showing inagglutinability by H antiserum, gave evidence of changes in O antigens, both quantitative in regard to those normally present, and qualitative in the sense that the findings suggested the presence of a new O component. *L. P. Garrod*

BRETSCHNEIDER, R., STUR, O. & ZWEYMÜLLER, E. Schwere Chloramphenicol-Nebenwirkungen bei reifen Neugeborenen und Frühgeborenen. Eine bei operierten Neugeborenen bisher unbekannte Todesursache. [**Severe Side Effects from Chloramphenicol in Full-Term and Premature Infants. A Hitherto Unknown Cause of Death in Infants subjected to Surgery**] *Deut. med. Woch.* 1960, Aug. 12, v. 85, No. 33, 1444–8, 1475, 1 fig. [15 refs.]

These authors from Vienna report 5 deaths during the administration of chloramphenicol to infants. The case

histories of 4 are given, the fifth being mentioned only briefly as differing from the rest. Of these 4 infants 3 were full-term: the other is said to have been 2 weeks premature (but weighed 3·7 kgm.).

The operations of ileostomy and colostomy respectively were done in 2 of the infants for meconium ileus: 1 had a congenital oesophageotracheal fistula which was treated first by oesophagostomy and then gastrostomy: 1 was a mongol with persistent vomiting on whom a laparotomy was done for supposed obstruction, although none was found. Chloramphenicol was given intramuscularly in doses varying from 87 to 117 mgm./kgm. per day. Sudden onset of circulatory collapse [the "grey syndrome" of American writers] occurred after some days, followed by death usually within a few hours. At post mortem all had either a "fibrinous peritonitis" [no bacteriological data] or bronchopneumonia or both.

The authors protest that their dosage of chloramphenicol did not exceed that recommended by the Council on Pharmacy and Chemistry of the American Medical Association in 1956 (100–150 mgm./kgm. daily) and refer to recent investigations in that country which afford an explanation of why these large doses may be fatal in the newborn [this *Bulletin*, 1960, v. 35, 907]: they also complain that a consequent recommendation to limit the dosage to 50 and 25 mgm./kgm. daily in full-term and premature infants respectively was sent by the manufacturers "only to doctors in the United States and Canada." [The authors may at least console themselves that their infants were in any case gravely ill. Fatalities reported from elsewhere have mostly been in infants treated prophylactically for doubtful indications, and not actually suffering from any known infection or other disease.] *L. P. Garrod*

Joy, R. J. T., Scalettar, R. & Sodee, D. B. **Optic and Peripheral Neuritis. Probable Effect of Prolonged Chloramphenicol Therapy.** *J. Amer. Med. Ass.* 1960, Aug. 13, v. 173, No. 15, 1731–4, 3 figs. [18 refs.]

The authors describe the occurrence of toxic optic and peripheral neuritis in a man aged 20 who was treated with chloramphenicol 3 gm. daily for 4 months. The authors consider the neuritis to be due to the chloramphenicol although apparently the patient also had novobiocin 3 gm. and sulfisoxole [sulphafurazole] 4 gm. daily for the same period. They refer to similar cases occurring after prolonged chloramphenicol therapy.

A. B. Christie

Kent, S. P., Tucker, E. S. & Taranenko, A. **The Toxicity of Chloramphenicol in Newborns versus Adult Mice.** *Amer. J. Dis. Children.* 1960, Sept., v. 100, No. 3, 400–404, 1 fig. [19 refs.]

"The toxicity of chloramphenicol has been studied in newborn and adult white mice. The lethal dose for 50% of newborn mice under the conditions of this experiment was found to be 315±22·6 mg. per kilogram per 24 hours, and the lethal dose for 50% of adult mice was found to be 1,675±35·6 mg. per kilogram per 24 hours or 5·3 times as much as the lethal dose for 50% of newborns. The desirability of toxicity studies on new drugs in newborns as well as adult experimental animals before their use in man is discussed."

Clapper, W. E. & Proper, R. **Comparative Activity of Demethylchlortetracycline and Tetracycline against Organisms commonly encountered in Clinical Material.** *Antibiotics & Chemotherapy.* New York. 1960, Aug., v. 10, No. 8, 473–8.

A plate dilution method was used to determine the minimum inhibitory concentrations of tetracycline and demethyltetracycline (DMCT) [this *Bulletin*, 1959, v. 34, 369, 655] for 247 strains of 13 varieties of bacteria. The relative activities of the two antibiotics are expressed, not in absolute values, but as a percentage of strains of each organism more sensitive to DMCT than to tetracycline and *vice versa*. Among 5 species of Gram-positive cocci, these figures were respectively 58 and 12% for *Staphylococcus aureus*: among 4 species of streptococcus none were more sensitive to tetracycline than to DMCT and varying percentages showed the opposite. The findings with 8 varieties of Gram-negative bacilli were similar, 60–82% of strains being more sensitive to DMCT than to tetracycline and only 0–14% showing the reverse: the single exception was *Haemophilus influenzae*, in which each difference occurred in 30%. A considerable proportion of some species were resistant to both antibiotics: the use of a disc containing 30 μgm. of tetracycline is recommended for distinguishing between resistance and susceptibility to both. A few observations on the bactericidal action of DMCT are also reported, and the results of some blood level determinations suggesting that 150 mgm. at 6-hour intervals is an adequate dose. *L. P. Garrod*

Snell, J. F. & English, A. R. **Radioactive Tetracycline. I. Effects of Glucosamine, Citric Acid, and Metaphosphate on Serum Levels.** *Antibiotics & Chemotherapy.* New York. 1960, Sept., v. 10, No. 9, 531–4, 2 figs.

"Tritium-labeled preparations of tetracycline with glucosamine, citric acid, and sodium metaphosphate were administered to beagles by stomach tube.

"After administration of the antibiotic, radioassays and bioassays were made from serum at regular intervals in order to determine the relative effectiveness of the potentiating substances on tetracycline serum levels.

"Results showed that significantly higher sustained serum levels were constantly achieved with glucosamine-potentiated tetracycline. This was clearly demonstrated in the data of over-all averages of ratios in both radioassays and bioassays. The comprehensive averages, likewise, were definitely higher in the glucosamine-potentiated tetracycline than in the other two tetracycline preparations."

ISENBERG, H. D., KARELITZ, S. & SMULEWICZ, Renata. **A Clinical and Laboratory Evaluation of Propionyl Erythromycin.** *Antibiotic Med.* New York. 1960, Aug., v. 7, No. 8, 502–9. [16 refs.]

These authors at the Long Island Jewish Hospital treated 98 patients, 30 carriers of streptococci or staphylococci and 6 "contacts," with propionyl erythromycin, with good results in 111 out of a total of 134. The patients are classified under 17 diagnoses, with only 1–5 patients in each except otitis media 10 (good result in 8), pneumonia 8 (8) and acute streptococcal pharyngitis 44 (36). Several tables give details of the organisms cultivated from these patients and of their sensitivity to erythromycin and 8 other antibiotics before and during or after treatment. [The various species are not related to the diagnoses, and some of them, such as 63 strains of *Streptococcus viridans* and many coagulase-negative staphylococci, are of doubtful pathogenicity.] Some apparent increase in bacterial resistance was observed during treatment, but never before the 10th day. The percentages of strains isolated before and after treatment and found resistant to erythromycin were: coagulase-positive staphylococci 11 and 27 respectively, coagulase-negative staphylococci 17 and 30, *Streptococcus pyogenes* 1·4 and 17, Group D streptococci 0 and 8, *Haemophilus influenzae* 20 and 30, *Neisseria* spp. 0 and 8, and *Str. viridans* 19 and 2·4. This last highly anomalous result is discussed but not convincingly explained.

L. P. Garrod

FORTUNATO, A., SEPE, E., TANCREDI, R. & ARA, F. Attività antibiotica delle miscele spiramicina-tetraciclina e spiramicina-C.A.F. su 100 ceppi di *Micrococcus pyogenes.* [**Antibiotic Activity of Spiramycin-Tetracycline and Spiramycin-Chloramphenicol Mixtures on 100 Strains of Staphylococci**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Mar.–Apr., v. 11, No. 2, 115–24, 2 graphs. [12 refs.]

The English summary appended to the paper is as follows:—

"The authors studied *in vitro* the bacteriostatic action of two antibiotics associations (spiramycin + tetracycline and spiramycin + CAF) on 100 strains of coagulase-positive Micrococcus pyogenes strains.

"Upon comparison with the activity of each of the two antibiotics alone, the spiramycin + tetracycline association proved to be the most effective."

JADIN, J. Activité bactéricide de l'association kanamycine-pénicilline. [**Bactericidal Activity of the Combination Kanamycin-Penicillin**] *Ann. Soc. Belge de Méd. Trop.* 1959, Dec. 31, v. 39, No. 6, 831–46.

Using a tube-dilution method the author determined the minimum inhibitory concentrations of pencillin, kanamycin and both together in different proportions, for 17 strains of staphylococci and 8 of various Gram-negative bacilli, including *Salmonella typhi.* Tubes showing no growth were sub-cultivated on agar to determine the concentration which was also bactericidal: this is said to have been usually twice the minimum inhibitory concentration (but little further reference is made to this feature of the tests, and the 14 tables appear to refer to the inhibitory concentrations only). Against almost all species the 2 antibiotics acted synergically in combination. This action was greatest against strains of penicillin-resistant staphylococci: *e.g.,* a strain not inhibited by 100 units/ml. of penicillin and inhibited by 12·5 μgm./ml. of kanamycin was inhibited by combinations of 12·5 and 0·78, and 3·1 and 1·56 respectively. Similar results, although with less extreme differences, obtained with *Salm. typhi* lead the author to suggest that this combination might be of value in eliminating this organism from carriers.

L. P. Garrod

SCHÖNENBERG, H. Klinische Erfahrungen mit dem neuen Antibiotikum Colistin. [**Clinical Results with Colimycin (Colistin)**] *Deut. med. Woch.* 1960, Sept. 23, v. 85, No. 39, 1714–17, 1742. [13 refs.]

The English summary appended to the paper is as follows:—

"Colistin (Colimycin: Chemie Grünenthal, Stolberg) was administered to 144 children with a variety of bacterial infections. Results were excellent in 88 premature and mature infants with E. coli enteritis. Good results were also obtained in 7 children with Sonne-E dysentery, although in one of them the causative organism was still demonstrable after the drug had been discontinued and the child was clinically improved. Colimycin, injected i.m., gave good results also in acute and chronic urinary infections due to E. coli, but recurrences could frequently not be prevented. The drug was also used in a limited trial on 7 infants and toddlers with pertussis, but no definitive conclusions could be drawn from this small series."

FLEISCHHAUER, G. Über Resistenzprüfungen und klinische Erfahrungen mit Colistin. [**Bacterial Resistance Studies and Clinical Results with Colistin**] *Deut. med. Woch.* 1960, Sept. 23, v. 85, No. 39, 1717–19, 1743. [28 refs.]

The English summary appended to the paper is as follows:—

"The resistance was tested of 122 bacterial strains (E. coli, coliforms, and Salmonella) to colistin, streptomycin, chloramphenicol and neomycin. Colistin seemed to be of particular value against bacteria which cause enteritis in infants. Clinically it proved to be well tolerated with low toxicity; it gave good results in 32 cases of enteritis in infants without recurrences. The action of neomycin and colistin in enterides without demonstrable bacterial cause is discussed."

HANKA, L. J. & BURCH, M. R. **Improved Assay for Psicofuranine.** *Antibiotics & Chemotherapy.* New York. 1960, Aug., v. 10, No. 8, 484–7, 2 figs. [11 refs.]

"An improved assay medium for psicofuranine was described. It was established that the liver extract, used in the early assays, was not necessary for manifestation of the in vitro activity."

[See this *Bulletin*, 1959, v. 34, 1156.]

GORZYNSKI, E. A., NETER, E. & COHEN, E. **Effect of Lysozyme on the Release of Erythrocyte-Modifying Antigen from Staphylococci and *Micrococcus lysodeikticus*.** *J. Bacteriology.* 1960, Aug., v. 80, No. 2, 207–11. [11 refs.]

HERRMANN, E. C., Jr. & ROSSELET, J. P. **Method for Detecting Antiviral Agents on Paper Chromatograms.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 304–6, 4 figs.

Chromatographic paper on which an antibiotic or other substance has migrated is laid for a short time on an agar layer covering a chick embryo cell culture inoculated with a virus. The presence and location of an antiviral agent are indicated by an area in which plaques due to virus multiplication do not form. Illustrations show this effect as produced on West Nile virus by "antibiotic W–112", the authors using different solvent systems and applying the chromatogram at different times after inoculation of the culture with virus. Experiments were also done with isatin-monothiosemicarbazone, which in this type of test, as in others, acts only on vaccinia virus: 20 μgm. of this substance were required to produce a plaque-free zone, but only 1 μgm. of antibiotic W–112. *L. P. Garrod*

HENNEBERG, G. & HÖPPNER, E. Desinfektionsversuche an Viren. [**Studies of Virus Disinfection**] *Arch. f. Hyg. u. Bakt.* 1960, May, v. 144, No. 3, 149–58. [10 refs.]

Virus-containing material from mice or eggs was dried on small pieces of fabric and immersed in different concentrations of 9 disinfectants for 1–360 minutes. The fabric was then removed and the disinfectant neutralized: material extracted from the fabric was then used to inoculate mice or eggs, of which 1,938 and 9,560 respectively were used in a series of tests embracing 4 viruses (psittacosis, vaccinia, mumps and influenza) and 9 disinfectants (formalin, chloramine, phenol, lysol, "cresol soap", chlor-m-cresol, Sagrotan and ethyl and propyl alcohol). The results are too complex for brief summary, but notable points in them are the high activity credited to alcohols (propyl alcohol, sometimes in as low a concentration as 20%, disinfected consistently in 1 or 2 minutes), and the poor activity of phenol and cresols against some viruses. The concentrations of formalin required to kill in periods of 2–30 minutes varied from 0·25% for influenza virus to 5% for mumps. There is little discussion of the results, but the authors remark that other workers have obtained conflicting results, which they attribute to the use of the "suspension" as distinct from the "carrier" method employed here. *L. P. Garrod*

GERMANOVA, K. I. & SAVEL'EVA, A. M. **The Inhibitory Effect of the New Antibiotics 1212 and 452–7 upon Vaccinia Virus.** *Problems of Virology.* London. 1959, v. 4, No. 3, 92–7, 3 figs. [Translated from Russian.]

This paper reports experiments on vaccinia virus with 2 antibiotics of actinomycete origin. They were tested by injecting them into the allantoic cavities of 11–12-day chick embryos 0–18 hours after the embryos were infected with massive doses of virus by the same route. The substance called 1212 was more active than 452–7. Both substances showed greater activity against small doses of virus. Administered 3 hours after infection, the efficiency of 1212 "hardly changes", while the inhibitory effect of "452–7 shows a considerable decrease". [There is some conflict (or uncertainty) between these statements and Fig. 1.] Injected 18 hours after infection both antibiotics were ineffective.

Both antibiotics showed *in vitro* virucidal activity. As in the *in vivo* tests, 1212 was more active than 452–7.

The *in vitro* reaction between antibiotics and virus was not temperature dependent. It seems from the published report that the *in vivo* effect is an extension of the *in vitro* virucidal or virustatic effect. It may be that these 2 antibiotics will turn out to be the same after further purification. *Colin Kaplan*

FREEMAN, M. A. R. & BARWELL, C. F. **Ethylene Oxide Sterilization in Hospital Practice.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 337–45, 1 fig. & 2 pls. [11 refs.]

For some time ethylene oxide has been used in the United States as a sterilizing agent and special equipment for its use has been commercially available. This paper describes an experimental ethylene oxide sterilizer which does not differ materially from these, except in the absence of automatic control gear. After preliminary evacuation to approximately 30 inches Hg. water was introduced to yield a relative humidity of 30–50%. A mixture containing 10% ethylene oxide and 90% Arcton 12 was run in until a positive pressure of 5 lb. per sq. inch was produced: after 14 hours the chamber was again evacuated to 30 inches Hg, atmospheric pressure was restored with sterile air and the load removed. The temperature was maintained at 30–40°C. and the effective concentration of ethylene oxide was 555 mgm. per litre.

A wide variety of heat sensitive objects were sterilized, including catheters, plastic prostheses, endoscopes, ball-point pencils, blankets and amniotic membrane. The effectiveness of sterilization was tested by using filter-paper discs on which various organisms were dried. Spores of *Bacillus subtilis* proved the most resistant, as has been the experience of other workers: 10^6 spores

were killed in 2–4 hours and the 14-hour periods used thus provides a generous margin of safety.

A novel feature of the technique described here is that the final vacuum was held for 2 hours. It was found that in certain materials, such as polyvinyl chloride (PVC) tubing, bubbles of gas were formed which were thought to be Arcton. It was also found that ethylene oxide dissolved in PVC could be removed by a vacuum of 30 inches Hg held for one hour.

Other investigations showed that the materials sterilized suffered no deterioration and that satisfactory penetration was achieved when goods were packed in PVC, polythene, nylon, cloth, cardboard and paper.

The authors conclude that ethylene oxide sterilization is reliable, simple and safe, but that because of its slowness and expense relative to steam it is not indicated for heat stable materials. *J. C. Kelsey*

BETTAUER, G., SCHNEEWEISS, U., PRZYBOROWSKI, R. & HORN, H. Versuche über die sporentötende Wirkung von siedenden wässrigen Formalinlösungen. [**Studies of the Sporicidal Action of Boiling Formalin Solutions**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* 1960, Mar., v. 6, No. 3, 172–7, 2 figs. [39 refs.]

An official instruction issued in Germany in 1954 prescribes boiling in formalin solution as a method of sterilization. These workers at the Humboldt University, Berlin, maintain that the method is ineffective. Their test objects were bags containing 3 gm. ground and dried garden soil: these were placed in flasks containing formalin in 9 different concentrations varying from 0·1 to 6%, and boiled for 6 periods from 5 to 30 minutes: the flasks had a reflux condenser to prevent loss of the germicide. After cooling, the bags were treated with ammonia, washed and cultivated aerobically in broth, incubation being continued for 12 weeks, although cultures apparently sterile after 4 days rarely showed growth later. In multiple tests the results were very irregular, and not clearly related either to formalin concentration or to the duration of boiling: the percentages of total cultures yielding growth from the 9 concentrations of formalin in increasing order (from 0·1 to 6%) were 56, 44, 22, 39, 28, 22, 39, 33 and 39.

[If such a crude method is to be used, in preference to determining the rate of killing of a pure spore suspension, does it not require a contamination control, *i.e.*, the performance of multiple identical tests with previously autoclaved bags of soil to determine how often contamination occurs during the various operations of neutralization, washing and transfer? The paper does not actually state that positive cultures always contained sporogenous bacilli only, or indeed whether they were examined microscopically: if in fact they never contained cocci the significance of the findings would be enhanced.] *L. P. Garrod*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

MOORE, B. **A New Screen Test and Selective Medium for the Rapid Detection of Epidemic Strains of *Staph. aureus*.** *Lancet.* 1960, Aug. 27, 453–8, 3 figs. [12 refs.]

During investigations of the ability of staphylococci to digest catgut, it was observed that the growth of some strains was inhibited by a batch of catgut that had been treated with mercuric iodide. Exploration of this finding revealed that, in a medium composed of 2% Oxoid peptone, 0·5% sodium chloride and 1% Davis agar, mercuric chloride at a concentration of 1 in 27,500 was able to inhibit the growth of many strains of staphylococci. Some strains were, however, quite resistant, and almost all of these belonged to phage types commonly reported as producing epidemics of infection in hospitals. In all, 505 strains isolated in various hospitals in south-west England were examined; 244 were mercury resistant. Of the resistant strains, 107 were type 80, 30 type 52/52A/80 and 69 fell into 3 phage-group III patterns commonly found in hospital epidemics. Only 6 type-80 and 1 of the 52/52A/80 strains in the material were mercury sensitive; sensitive strains were however more common among the group III "epidemic types". There was no direct correlation between mercury sensitivity and antibiotic resistance on the egg yolk reaction.

[The importance of this observation lies in the suggestion that mercury resistance is correlated not with ability to produce disease, but with ability to produce epidemics of infection. It is thus potentially of very great usefulness.] *R. E. O. Williams*

GLADSTONE, G. P. & GLENCROSS, E. J. G. **Growth and Toxin Production of Staphylococci in Cellophane Sacs *in vivo*.** *Brit. J. Exper. Path.* 1960, June, v. 41, No. 3, 313–33, 13 figs. (2 on pl.). [21 refs.]

21 coagulase positive and 7 coagulase negative strains of staphylococci were grown in Cellophane sacs in the peritoneal cavity of rabbits, guineapigs, mice and rats; not all strains were tested in each animal species. The sacs were equipped with a device for sampling *in situ* which allowed the growth curves and production of α-haemolysin, PV leucocidin (both "fast" and "slow"

components [WOODIN, *Biochem. J.*, 1959, v. 73, 225]) and coagulase to be estimated. One coagulase positive strain (phage type 80) and 4 coagulase negative strains gave little or no growth in 24 hours in rabbits, but all strains grew well in mice. Of the 4 coagulase negative strains which failed to grow in 24 hours, 2 grew after 48 hours. Re-inoculation from this growth into a fresh sac in a second rabbit gave good growth overnight. This and other experiments suggested that mutants adapted to growth in the rabbit were being selected. Growth curves *in vivo* (rabbit, mouse and guineapig) of 3 coagulase positive strains were compared with similar curves *in vitro* (rabbit serum diffusate medium). Mean generation times *in vivo* were 2-fold or greater than those *in vitro*. These differences did not appear to be due to temperature differences, oxygen supply or the presence or absence of lysozyme but evidence is presented that diffusible inhibitory factor or factors are present in inflammatory exudate but absent from serum.

High yields of α-haemolysin and the "fast" and "slow" components of PV leucocidin were produced by 4 coagulase positive strains growing *in vivo* (mice, rabbits, guineapigs and rats) in 24 hours. Similar cultures *in vitro* growing in rabbit serum diffusate or inflammatory exudate produced no haemolysin and negligible amounts of PV leucocidin; in yeast-casein-hydrolysate medium, which is optimum for leucocidin production *in vitro* (*loc. cit.*) the strains produced 5–50% of the *in vivo* yield of leucocidin. Coagulase positive strains which were non-haemolytic *in vitro* produced α-haemolysin *in vivo* but coagulase negative non-haemolytic strains failed to do so. Some strains produced coagulase *in vivo* but the yield was no greater than *in vitro*. In view of the results it is pointed out that tests for toxigenicity on cultures grown *in vitro* may not always be valid.

H. Gooder

MAZLOUM, H. A. **The Slide Microtest for Gelatin Liquefaction in Staphylococcus and Proteus Spp.** *J. Egyptian Med. Ass.* 1960, v. 43, No. 4, 222–34.

A micro test involving the use of a thin layer of gelatin on a microscope slide was not as good as the classical "tube" test for determining gelatinase production by staphylococci; it could be used as a substitute with strains of *Proteus*.

R. E. O. Williams

GHITTER, Leah R.; WOLFSON, S. W. **A Simplified Approach to the Phage Typing of *Staphylococcus aureus*. I. The Use of Lyophilized Phage** [GHITTER & WOLFSON]. *Amer. J. Clin. Path.* 1960, July, v. 34, No. 1, 77–91. [49 refs.] **II. A Mechanical Adjunct to the Typing Procedure** [WOLFSON & GHITTER]. *Ibid.*, 92–4, 4 figs. [Reprinted from *Tech. Bull. Registry Med. Technol.* 1960, June, v. 30, 93–107; 108–10.]

I. The authors believe that staphylococcal phage typing could be simplified by lyophilization of the typing phages so that reconstitution gives a preparation suitable for routine use.

Having described their method for preparation of phages, which is said in some cases to give preparations with a critical test dilution (CTD) of 10^{-8}, they give a table showing the drop in titre after storage at 4°C., but the rate of fall in column 5 is not expressed as a K value. [Presumably side reactions in the last column refer to additional reactions with these phages at CTD on the strains used in propagation of the other phages. If this is the case many of the phages have host ranges so different from the phages in use in most laboratories that they would not be considered acceptable.]

Phage filtrates varied in their stability, phage 55 showed no drop after 9 weeks' storage while 44A showed a 3-log drop, and 3A a 2-log drop, after 2 weeks' storage. [The authors do not state how many preparations of each phage were tested in this way. The abstracter has not found a drop of more than 1 log over 5 years of storage except in the case of contaminated material. A small drop occurs with some phages *e.g.* 42D, but 3A would not be considered a phage liable to drop in titre on storage.]

Preparations lyophilized to give an estimated CTD on reconstruction with distilled water were then compared with liquid phage over a 4-week period. How this comparison was made is not clear from the text, but the variations in both preparations are in many cases too wide for either to be used in routine work [the "cross reactions" do not correspond with those given for the same phages in the previous table].

The authors state that in some cases the lyophilized phage had a slightly lower initial titre owing to loss during lyophilization, and in order to compensate for this "each concentration prior to lyophilization is adjusted to its viability following the lyophilization procedure". No experiments are reported to show that this loss is constant with a particular batch or a particular phage.

[There may well be advantages to using lyophilized preparations if they are reliably shown to be more stable than lysates held at 4°C. but the work described here does not establish that the materials could be used without checking each preparation.]

II. An apparatus is illustrated and described for delivering drops of phage on to a typing plate for routine staphylococcal typing. A series of cartridges containing phage filtrate are slotted through a metal plate so that their rubber tops protrude. The plate is slipped into the apparatus so that pressure on to a spring-loaded plate expels a drop of phage from the bottom of each cartridge through a fine needle, on to a plate flooded with the test strain.

The advantage of the apparatus in the authors' opinion is that cartridges can be prepared containing lyophilized phage which could be rehydrated for use as required. If, as the abstractor believes, titration of the material in each cartridge would be necessary before use, this advantage disappears although the cartridges could of course be filled with fluid phage at CTD before use.

[The abstracter, who has had an opportunity to try this machine, experienced some difficulty in adjusting the

apparatus so that each cartridge delivered one drop and Fig. 2 suggests that this is a common difficulty as some clearings appear larger than others, suggesting that 2 drops were in fact dispensed. This difficulty, however, could probably be overcome with practice.]

The arrangement of drops in 2 circles makes positioning difficult but the illuminated viewbox makes the reading of plates considerably easier.

M. Patricia Jevons

ROZANSKY, R., WELLISCH, G., HALEVI, Cila & BIRNBAUM, D. **A Comparative Antibiogram of Strains of Coagulase Positive Staphylococci isolated from Different Sources.** *Bull. Res. Counc. of Israel.* 1960, Apr., v. 8E, No. 3, 105–8, 2 figs. [14 refs.]

Coagulase-positive staphylococci isolated from purulent lesions from out-patients and in-patients of the Hadassah University Hospital, Israel, during the first half of 1959 were compared. They were tested for their sensitivity to penicillin, streptomycin, aureomycin, terramycin [oxytetracycline], chloramphenicol, erythromycin, oleandomycin, bacitracin and novobiocin by the disc method.

In-patient strains were less sensitive than out-patient strains but the order of sensitivities was similar, 30% of out-patient strains were penicillin sensitive (nearly twice as many as in-patient strains) and between 60 and 70% were sensitive to terramycin. Nearly 100% of strains from both groups were sensitive to novobiocin.

The antibiogram of strains from 60 infants from the maternity department showed that 99% were penicillin resistant, 90% resistant to streptomycin, terramycin, 70% resistant to erythromycin, 50% resistant to chloramphenicol; as in the other groups the majority of strains were sensitive to novobiocin which is not in general use in Israel. Strains of the same antibiotic pattern were also isolated from the staff of the maternity department.

M. Patricia Jevons

BLOBEL, H., BERMAN, D. T. & SIMON, J. **Purification of Staphylococcal Coagulase.** *J. Bacteriology.* 1960, June, v. 79, No. 6, 807–15, 5 figs. [13 refs.]

Non-haemolytic mutants of two potent coagulase-producing strains of staphylococci (designated T and A168) were selected after 8 cycles of alternate platings on fibrinogen medium and blood agar. After growth of the mutants, in heart infusion broth for 5 days on a rotary shaker, the free coagulase in the broth was purified by removal of the cells, precipitation at *p*H 3·8, 2 precipitations by ethanol (final concentration 70%) and finally starch column electrophoresis. This preparation contained 20,000 minimal clotting doses per mgm N. Injection of the purified coagulase in rabbits stimulated the formation of coagulase inhibiting antibodies [*cf.* this *Bulletin*, 1958, v. 33, 1177.] *H. Gooder*

CASMAN, E. P. **Further Serological Studies of Staphylococcal Enterotoxin.** *J. Bacteriology.* 1960, June, v. 79, No. 6, 849–56, 1 fig.

Rabbit antisera prepared against the enterotoxin of staphylococcal strains S6 and 196E were used to develop a specific serological test (based on the Ouchterlony type of agar diffusion method) for 2 antigens present in staphylococcal cultures that were associated with heat-resistant enterotoxicity. Of 22 strains of staphylococci capable of producing enterotoxin (as determined by the cat test [this *Bulletin*, 1959, v. 34, 384]) only 14 strains (all originating from cases of food poisoning) produced emesis in cats when heated culture filtrates were injected. 13 of these 14 strains elaborated the 196E type of antigen.

A study of 14 strains of staphylococci isolated from cases of enteritis showed 11 strains to produce antigens of the 243 type and 196E type of enterotoxin. 51 strains of staphylococci that did not produce heat-resistant enterotoxin produced neither of the type antigens. "It is suggested that the 'food-poisoning enterotoxin' associated with the 196E type of antigen be referred to as 'type F' and that, because of its production by most of the strains of 'enteritis' origin the one associated with the 243 type antigen be designated 'type E'." Some strains produced a heat susceptible substance which was emesis inducing and apparently dialysable.

H. Gooder

SNAVELY, J. G. & BRAHIER, Jeanne. **The Viability of Streptococci under Field Screening Conditions.** *Amer. J. Clin. Path.* 1960, June, v. 33, No. 6, 511–15.

The authors investigated current methods of screening throat swabs from β-haemolytic streptococci preliminary to a large scale programme of prophylaxis of rheumatic fever by penicillin treatment of streptococcal infections.

Cotton tipped swabs were used and all swabs were plated on 5% sheep's blood agar plates incubated 35 to 37°C. Results were given on macroscopic examination of plates after 24–48 hours (occasional doubtful colonies were filmed or subcultured) and no grouping or typing was carried out. 4 methods were compared.

I. 100 swabs were collected and plated within 3 hours and an equal number were plated after being sent in paper envelopes by post.

II. All throat swabs received routinely in the authors' laboratory were compared with routine specimens received by other laboratories.

III. Duplicate swabs were taken from 490 patients—one was plated immediately and one after being sent by post.

IV. 300 consecutive single swabs were investigated more thoroughly. They were plated and examined as before. The same plates were then examined by an independent bacteriologist and positive reports only recorded after filming and subculturing all suspicious colonies. Swabs were then inoculated into thioglycolate broth, 2 loopfuls of which were incorporated into poured blood plates after 1 hour's incubation.

No differences were observed between control and test plates in series I or those from the authors' laboratory in series II (21–24% positive). Comparison of results from other laboratories proved impossible owing to variation in technique and numbers of specimens.

Of 490 duplicate swabs in series III there were 15 discrepant pairs, in 8 the mailed specimen was negative and in 7 the immediately plated specimen was negative, suggesting faulty collection of specimen.

Microscopic examination and subculturing of colonies in series IV did not increase the number of specimens reported positive.

The authors conclude that β-haemolytic streptococci can be identified by their colonial appearance and that there is no decrease in the number isolated if the plating of swabs was delayed by 24–120 hours, [see also Hollinger *et al.*, this *Bulletin*, 1960, v. 35, 1033].

M. Patricia Jevons

Hook, E. W., Wagner, R. R. & Lancefield, Rebecca C. **An Epizootic in Swiss Mice caused by a Group A Streptococcus, Newly Designated Type 50.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 111–19, 2 figs. [15 refs.]

"This report describes a widespread naturally occurring outbreak of group A streptococcal infections in a colony of Swiss albino mice. Streptococci were cultured from the throats of 22 per cent of weanling mice, 34 per cent of adult mice and 52 per cent of breeders. One third of infected mice developed signs of cervical lymphadenitis, and approximately 50 per cent of mice observed for 3 months died of systemic streptococcal infection. All features of the naturally acquired disease could be reproduced by deposition of streptococci in the nares of mice formerly free of infection.

"The group A streptococcus responsible for the present epizootic has been shown to belong to the same serologic type as streptococci isolated from 3 other outbreaks of infection in laboratory mice and has been newly designated group A, type 50."

Michel, M. F. & Hijmans, W. **The Additive Effect of Glycine and other Amino Acids on the Induction of the L-Phase of Group A β-Haemolytic Streptococci by Penicillin and D-Cycloserine.** *J. General Microbiol.* 1960, Aug., v. 23, No. 1, 35–46, 1 fig. & 1 pl. [24 refs.]

Glycine, when tested alone, did not induce L-phase growth of group A beta-haemolytic streptococci. However, in the presence of penicillin, glycine, in a bacterial inhibitory concentration, brought about a sharp increase in the yield of L-phase colonies compared with penicillin alone. A similar effect was observed when serine, threonine, methionine or alanine were substituted for glycine. In most cases the D-isomer was the active form of the amino acid. D-cycloserine had a weak effect in inducing the L-phase on group A streptococci when used alone and the combined effect of D-cycloserine and glycine or DL-serine was equal to that obtained with penicillin and the same amino acids. *H. Gooder*

Reed, R. W. & Matheson, B. H. **Experimental Nephritis due to Type Specific Streptococci. IV. The Effect of Type 12 Nephrotoxin in Monkeys.** *J. Infect. Dis.* 1960, May–June, v. 106, No. 3, 245–9, 12 coloured figs. on 2 pls.

9 monkeys were each given 4 intravenous injections of the polypeptides prepared from type 12 streptococcal cultures and found in earlier work to produce nephritis in rabbits [this *Bulletin*, 1955, v. 30, 173]. No clinical investigations or urine analysis were made but the monkeys were killed at intervals and their kidneys examined histologically. 24–30 days after the start of the injections, several monkeys showed marked congestion of the glomeruli. In kidneys from monkeys killed later there was proliferation of the capsular epithelium and thickening of the basement membrane. In the later stages there was marked fibrosis. [There is no indication of the proportion of the glomeruli that showed the changes.] *R. E. O. Williams*

Zaglukhinskaia, E. N. **The Effect of Mycerin on Various Types of Pneumococcus.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 76–9. [Translated from Russian.]

This paper has nothing to say about the general properties of mycerin, except that it is a new antibiotic, but records the interesting fact that different types of pneumococcus are sensitive to it *in vitro* to varying degrees: type IX is inhibited by 2·5 μgm./ml., and types I and VI by 5 μgm./ml., but types II and IV not by 30 μgm./ml. Therapeutic tests in mice, inoculated intranasally and treated by 2 daily subcutaneous injections of antibiotic, gave unexpected results: these were best in type IV infection (one of the 2 most resistant types), the animals not only recovering but their organs being sterilized. Lesser degrees of therapeutic effect were obtained in infections by some other types. [The results are less conclusive because not all controls died in any experiment, and type IX, the most sensitive organism, was almost avirulent.] *L. P. Garrod*

Schwarz, H. Zur Züchtung boviner Tuberkelbakterien auf Blutagar. **[Isolation of Bovine Tubercle Bacteria on Blood containing Media]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 506–14. [40 refs.]

The medium used was that of Tarshis which consists of glycerine agar containing 25% of donor blood with sterilizing fluid and 500 units penicillin/ml.

Better results were obtained in respect of speed and abundance of growth, and number of positive cultures, with this medium, provided glycerin was omitted, than with the egg media of Löwenstein–Jensen and Petragnani–Witte. The test was carried out with material from 120 lymphatic glands from tuberculous animals and with 40 samples of milk positive by microscopic examination. The samples were treated with 3·75% HCl for 15 minutes before inoculation.

A variety of animal bloods proved equal to human blood for the preparation of the medium.

J. W. McLeod

ROBSON, J. M., SMITH, J. T. & THOMAS, C. G. A. **Multiplication of *Mycobacterium tuberculosis* in the Cornea and its Modification by Immunity and by Isoniazid.** *Amer. Rev. Respiratory Dis.* 1960, Aug., v. 82, No. 2, 195–201, 6 figs. [13 refs.]

In this paper the authors describe 2 main experiments, using the methods they have used and described previously. In the first experiment the corneal lesions, developing from the injection of 5 x 10^5 bovine tubercle bacilli, reached a miximum size in about 2 weeks and the total number of bacilli increased to approximately 10^7. The size of the lesion and the total number of bacilli then remained constant although the number of viable bacilli decreased by half every 55 hours for 24 days, after which it too became more or less stabilized.

In the second experiment half of the mice were immunized by the injection of 0·01 ml. of 10^{-3} dilution of a Dubos culture of the tubercle bacilli intradermally, given 1 month before the intracorneal injection; after challenge half these mice and half the control unimmunized mice were treated with 0·3 mgm. isoniazid daily in the food. In the vaccinated mice, irrespective of whether they were given chemotherapy or not, there was no initial increase in the total number of bacilli in the cornea, whereas in the unvaccinated mice chemotherapy had only a slight retarding effect on the initial increase. In the vaccinated mice there was a decrease in the number of viable bacilli but it was less than that which occurred from the 14th day onward in the unvaccinated mice. As in the first experiment the number of viable bacilli in all the mice became stabilized after about 4 weeks. In general, the lesions in all the vaccinated and the treated animals were smaller than those in the control mice. [The fact that those in the unvaccinated mice, treated with isoniazid, were similar to those in the vaccinated mice, in spite of a higher bacillary population, is attributed to an anti-inflammatory property of the drug.]

In discussing these results the authors point out that there is evidence from previous experiments to show that immunity begins to develop immediately after infection, but the fact that in the present experiments stabilization of the lesion and the fall in the number of viable bacilli begins only after the 14th day in the unvaccinated mice suggests that the lethal effect of immunity develops only after this interval. Why the lethal effect does not continue to act and completely eliminate the bacilli is unknown unless the residual bacilli become resistant, and the authors are investigating this possibility.

S. R. M. Bushby

RUSSELL, Ruth L., JANN, G. J. & FROMAN, S. **Lysogeny in the Mycobacteria. I. The Establishment of Lysogeny.** *Amer. Rev. Respiratory Dis.* 1960, Sept., v. 82, No. 3, 384–93, 2 figs. [32 refs.]

"Natural lysogeny could not be demonstrated in thirty-four stock cultures of representative saprophytic and pathogenic mycobacteria with no previous history of laboratory exposure to mycobacteriophage. It has been demonstrated that a number of these strains can be lysogenized by exposure to lytic or temperate mycobacteriophage under laboratory conditions. Phage-induced alterations in cultural or biochemical reactions were not detected among the lysogenized strains. Lysogenic cultures of *M. tuberculosis* H37Rv and *M. fortuitum* are virulent and remain lysogenic through animal passage."

BRAUN, A. Zur Praxis der Typenbestimmung von *Mycobacterium tuberculosis.* [**Practical Aspects of Typing *Mycobacterium tuberculosis***] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 1, 79–93. [28 refs.]

MATTMAN, L. H., TUNSTALL, L. H., MATHEWS, W. W. & GORDON, D. L. **L Variation in Mycobacteria.** *Amer. Rev. Respiratory Dis.* 1960, Aug., v. 82, No. 2, 202–11, 11 figs. [35 refs.]

This paper summarizes a 4-year investigation into the ability of mycobacteria to produce L forms. Of the successful methods used for other organisms, only hypertonicity induced by adding 0·35–0·7 M sucrose to the medium proved effective for human, bovine and avian tubercle bacilli, although adding 0·5 M sodium chloride gave sporadic success. In the presence of this sugar the more fastidious mycobacteria grew rapidly in 2 days in the L form on a synthetic medium and on nutrient agar. Penicillin in high concentration, applied to the medium on filter paper strips, provoked growth in this form in situations in which otherwise it was not found; dihydrostreptomycin inhibited the L forms and isoniazid modified the colonial form. Growth was best under decreased oxygen tension; increased CO_2 tension had no definite effect. Of the vitamins, only nicotinamide fostered growth, and even that was not essential. Serum was not essential but it may detoxicate some unsatisfactory batches of agar. The age of the culture used for the inoculum was not critical.

The L cycle for mycobacteria is essentially the same as for other bacteria. Giant forms 100–150 μ develop and these produce filaments and filterable granules; the colonial forms are very pleomorphic. Transfer experiments with *Mycobacterium avium* showed that the L forms reverted to the bacillary forms when transferred to Löwenstein and Petragnani media but not when transferred to nutrient agar or the synethetic medium. The examination under phase-contrast microscopy of cerebrospinal fluid and sputa from patients with tuberculosis showed the presence of forms which resembled the fungoid and granular types of L colonies.

The authors consider it reasonable to assume that MUCH granules and other atypical forms of the tubercle bacillus seen *in vivo* are L forms. *S. R. M. Bushby*

BARUA, D., NAIK, U. P., AIKAT, B. K. & BASU, A. K. **Bacteriological Study of Resected Tuberculous Lungs.** *Indian J. Med. Res.* 1960, May, v. 48, No. 3, 263–75, 1 graph. [36 refs.]

This report is based on the examination of 216 different lesions obtained from 52 patients who had

extremely variable regimens of domiciliary treatment with PAS, streptomycin and isoniazid, and whose ages ranged from 17–55 years.

In 44 patients acid-fast bacilli were demonstrated in smears of contents of the lesions but from 23 of these no bacilli were recovered by culture or guineapig inoculation; from 2 patients the bacilli were demonstrated in the guineapig but not in culture; from 4 patients the reverse occurred and these cultures failed to produce progressive disease when injected into guineapigs and they were catalase-negative, neutral-red positive, and resistant to 100 μgm. isoniazid per ml. No correlation was found between these results and the drugs used or their duration of administration, and the viability varied in different lesions of the same specimen.

Viable bacilli were recovered from 75% of circumscribed lesions with liquefying material in them, from 48·5% of the cavernous lesions, from 16·7% of the caseous lesions, from 3·7% of the inspissated lesions and from 1 of the 5 calcified lesions.

6 strains from 3 patients were resistant to PAS, isoniazid and streptomycin; none of the strains was resistant to PAS only, although there were strains resistant to either streptomycin or isoniazid alone. Although incubation of the primary cultures was for 16 weeks, all the strains grew within 8 weeks.

Because the lesions from which the neutral-red positive, avirulent strains were isolated showed histological evidence of activity, a positive neutral-red reaction may be a better indication of virulence than the guineapig. *S. R. M. Bushby*

Tsukamura, M. & Yamamoto, M. **Genetic Studies on the Viomycin Resistance of *Mycobacterium tuberculosis*.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 355–64. [11 refs.]

Niffenegger, J. & Youmans, G. P. **The Effect of Macrocyclon on the Multiplication of Tubercle Bacilli in the Lungs and Spleen of Mice.** *Brit. J. Exper. Path.* 1960, Aug., v. 41, No. 4, 403–13, 7 figs. [23 refs.]

There is much evidence which strongly suggests that the non-ionic surface-active agent, macrocyclon (a polyethylene glycol ether of *p-tert*-octylphenol-formaldehyde cyclic tetramer) favourably affects the course of experimental tuberculosis by altering the tubercle bacillus so that it is more amenable to the destructive mechanisms of the macrophage [this *Bulletin*, 1955, v. 30, 752]. The present paper describes experiments designed to give information as to when and to what extent the multiplication of the tubercle bacillus is affected by the treatment.

Mice were infected intravenously with H37Rv and the macrocyclon was administered intraperitoneally, some of the mice being vaccinated with BCG before infection. At weekly intervals mice of each of the groups were killed and viable counts made on the number of tubercle bacilli present in the lungs.

The results of the first experiment showed that 25 mgm. of the macrocyclon given 25 hours before infection markedly suppressed the multiplication of the bacilli after the 7th day and prolonged the survival time of the mice. The results of the second experiment showed that even when the treatment was given 28 days before infection, it still had a similar although less pronounced effect, the effect then being of the same order as that afforded by vaccination. The third experiment was similar to the second, except that bacillary counts were also made on the spleens, and although in this experiment the suppression in the lungs was less, there was similar suppression in both organs.

In discussing these results the authors emphasize (1) the similarity of the behaviour of tubercle bacilli in the vaccinated mice and in the treated mice, and (2) that suppression of growth occurs at the stage when many of the bacilli in untreated mice become extracellular owing to breakdown of the macrophages. Macrophages from immune mice and from mice treated with Triton WR 1339 have been shown to be more resistant to ultrasonic vibration [*ibid.* 1959 v. 34, 815] and therefore this increased resistance may account, at least in part, for the eventual suppression of growth of the bacilli *in vivo*.

S. R. M. Bushby

Hart, P. D'A. & Rees, R. J. W. **Effect of Macrocyclon in Acute and Chronic Pulmonary Tuberculous Infection in Mice as shown by Viable and Total Bacterial Counts.** *Brit. J. Exper. Path.* 1960, Aug., v. 41, No. 4, 414–21, 2 figs. [24 refs.]

The authors consider this paper complementary to the one by Niffenegger and Youmans [see above]. In the experiments described, total and viable counts were made on the number of tubercle bacilli in the lungs of mice with acute and chronic experimental tuberculosis and treated with macrocyclon. The mice were infected intravenously with H37Rv and at intervals some of each group were killed for the counts; the total counts were made by the method of Hobby *et al.* (*Amer. Rev. Tuberculosis*, 1954, v. 69, 173).

In the acute infections, in which the median survival time of the untreated mice was 18–21 days, both the total and viable counts continued to rise so that by the 20th day they had increased from 10^6 to 10^9 bacilli per lung. In the mice treated with 25 mgm. macrocyclon twice weekly, the number of bacilli increased more slowly so that by the third week it was only 5×10^7, after which it became static. In the chronic infection, in which only 30% of the mice died within 8 weeks, there was no appreciable increase in the number of bacilli in either the treated or untreated mice.

The drug would therefore appear to be bacteriostatic in acute infections but to be ineffective in chronic infections, presumably because there is little or no multiplication of the bacilli. *S. R. M. Bushby*

Junghans, Ruth. Über die Di-Toxin-Bestimmung unter besonderer Berücksichtigung des mitis-Typs. [**Di-Toxin Determination with special consideration to the mitis-Type**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 496–505. [14 refs.]

The author has brought forward a number of observations on toxin determination with strains of diphtheria

bacillus of different cultural types. Of the 3 methods available for toxin determination, animal experiment, the lethal effect on the chick embryo and the agar diffusion test of OUCHTERLONY and ELEK she has found the last the most satisfactory.

From her own work and a review of the literature the main conclusion which can be drawn is that among the *gravis* strains there is considerable uniformity, about 80% give a positive test for toxin production: with the *mitis* strains it is otherwise. The percentage of *mitis* strains which are found toxigenic varies widely with the period and the place in which they are collected. This variation ranges from 10% to over 80%.

Pursuing this question, she has submitted a considerable collection of strains to repeated tests for toxigenicity, using successive subcultures on Löffler's serum medium. With few exceptions the *mitis* strains in such experiments lost their toxigenicity rapidly on repeated passage, whereas, again with few exceptions, the *gravis* strains retained their toxigenic quality. The strains which could not be typed tended to fall in line with the *mitis* strains. It is suggested that the explanation of these diverging results may be due to the B factor of O'MEARA [this *Bulletin*, 1947, v. 22, 349] in the toxic products of the *gravis* strains. No direct experimental evidence in favour of such a suggestion is submitted. *J. W. McLeod*

GÄRTNER, H. & KNOTHE, H. Über das Auftreten von C. pyogenes bei scharlachähnlichen Erkrankungen und Eiterungen beim Menschen. (Bericht über acht Isolierungen bei entsprechenden Fällen.) [**The Appearance of *C. pyogenes* in Human Cases of Illnesses and Suppuration suggestive of Scarlet Fever. (Account of 8 Isolations in such cases)**] *Arch. f. Hyg. u. Bakt.* 1960, June, v. 144, No. 4, 308–17. [19 refs.]

A small series of cases of infection with *Corynebacterium pyogenes* in human patients which occurred in the Kiel area is described.

2 of these were from purulent fistulae, 2 from the throats of healthy contacts and 1 from a follicular tonsillitis, and the remaining 5 from mild cases of angina associated with erythematous general body rashes suggestive of scarlet fever. The strains corresponded closely in their biochemical reactions and animal pathogenicity with those of a strain derived from the infected udder of a cow. The outstanding features were strong β haemolysis on blood agar, fermentation of saccharose and starch and high pathogenicity for guineapigs with manifestations of local suppuration and pyaemia.

Such infections apparently occur chiefly in children living in country districts and may, it is suggested, account for occasional cases of scarlatina in which β haemolytic streptococci cannot be isolated from the throat. *J. W. McLeod*

SHIFRINE, M. & BIBERSTEIN, E. L. **A Growth Factor for *Haemophilus* Species secreted by a Pseudomonad.** [Correspondence.] *Nature.* 1960, Aug. 13, v. 187, 623.

Extracts of supernates from cultures of a pseudomonad isolated from an emperor penguin have been shown to contain a growth factor for some *Haemophilus* strains (*H. influenzae, H. parainfluenzae, H. parahaemolyticus* and *H. gallinarum*).

After chromatographic separation, the ultra-violet-absorbing material (EP) was found to contain the growth factor. Species of *Haemophilus* require for growth, either the V factor—replacable with diphosphopyridine nucleotide or its nucleoside—X factor—replaceable with haem, or both. Since most of the animal *Haemophilus* strains stimulated by EP showed no haem requirement, a relationship between EP and diphosphopyridine nucleotide was suggested. Further purification and analysis suggest that EP might be a niacinamide riboside with unknown substitutions. *F. T. Perkins*

KASHAIEVA, A. A., KIRITSEVA, A. D., LIBINZON, A. E. & AVRorova, R. I. **Experimental Active Anti-Pertussis Immunity.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 54–60. [11 refs.] [Translated from Russian.]

The routine method of assay for pertussis vaccines is by single intraperitoneal injection of mice followed by subsequent testing of immunity to intracerebral infection. This method is unsatisfactory not only because it provides no standardization of the preparations used, but also because it fails to assess the ability of the vaccine to protect the respiratory tract.

In this paper it is shown that resistance of mice as determined by intracerebral infection appeared more rapidly and more easily than resistance as determined by infection of the respiratory tract. Immunity against subsequent intracerebral infection was achieved for 4 out of 8 strains of *Haemophilus pertussis* by single subcutaneous injection both of live and dead organisms: with smaller doses the rapid development of transitory resistance was demonstrated. Resistance of the respiratory tract was achieved only by two subcutaneous injections of live *H. pertussis.*

This paper confirms the findings of previous workers that the mechanism of protection of the respiratory tract against *H. pertussis* would appear to differ from that of the brain. *Constance A. C. Ross*

WILLIS, A. T. & GOWLAND, G. **Egg-Yolk Reactions of *Pseudomonas* Species.** [Correspondence.] *Nature.* 1960, July 30, v. 187, 432–3.

This short note reports the cultural reactions of 30 strains of *Pseudomonas* when grown on egg-yolk agar and other lecithin and fat-containing media. There were 15 strains of *Pseudomonas pyocyanea,* isolated from human infections, the remaining cultures belonged to other species of *Pseudomonas.* All strains were examined for lipolytic activity by growing them on fat-containing media (tributyin agar (Oxoid), cream agar, mono-stearate and tri-stearate agar) and for lecithinase activity by growing them on egg-yolk and also lecithin agar. The *Ps. pyocyanea* produced marked clearing on tributyin

agar and obvious lipolysis on cream agar and also on the mono- and the tri-stearate agar. They were all proteolytic on milk agar, mostly phosphatase-positive and pathogenic for mice. On lecithin agar and egg-yolk agar there was marked opalescence. The reactions of the *Pseudomonas* other than *Ps. pyocyanea* varied considerably. In general, however, those growing at 37°C. behaved like *Ps. pyocyanea,* whereas those growing at 25° and not at 37°C. were comparatively inactive.

This is in the nature of a preliminary report and further investigations are in progress . *H. J. Bensted*

KÖHLER, W. & HUBRIG, T. Über eine neue serologische Gruppe (h) bei *Pseudomonas aeruginosa.* [**On a New Serologic group (h) of *Pseudomonas aeruginosa***] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Oct., v. 120, No. 131–7.

VELAUDAPILLAI, T. **Transduction *in vivo*.** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 5, 470–80, 1 fig. [15 refs.]

This paper describes the application of the orthodox *in vitro* methods for the transduction of antigens in the *Salmonella* group to experiments with embryonated hens' eggs and mice. The phage lysates were prepared in the usual way by propagating phage P22 on the donor culture. The mixture of the lysate and the recipient bacterium, in the case of the living chick embryo, was inoculated either onto the chorio-allantoic membrane or into the yolk sac of 16-day-old eggs. A similar procedure was followed with the mice by injecting the mixture, variously diluted, intraperitoneally into white Swiss mice. The inoculated chick embryos were incubated for 24 hours before cultures were taken from the heart, allantoic fluid and the chorio-allantoic membrane. Mice were killed on the 7th day and cultures obtained from the heart and intestines. All the cultures were first incubated in tetrathionate broth for 24 hours before being mixed with nutrient agar and layered over soft agar containing the appropriate antiserum for the suppression of the homologous phase and to facilitate the recognition of the transduced phase.

Transductions and lysogenic conversions were equally successful in embryonated eggs and mice whether or not the mixtures were pre-incubated before inoculation. They were also successful when the lysates were inoculated 5 hours after the cultures. In addition transductions were obtained when a similar procedure was followed with non-embryonated eggs by inoculation into the albuminous fluid after some of it had been sampled to show that the egg was not contaminated with salmonellae. *H. J. Bensted*

BOKKENHEUSER, V. **The Interpretation of the Vi-Tests.** *South African Med. J.* 1960, July 16, v. 34, No. 29, 601–4, 1 fig. [24 refs.]

This is an attempt to evaluate the Vi-agglutination test as an indication of the typhoid carrier state in healthy persons whose blood sera show the presence of Vi agglutinins. The author's own experience with the test appears to have been disappointing, and he has selected from the extensive literature on the subject, in which opinions regarding the value of the test are very variable, 11 papers for analytical treatment of the results reported. In all these papers the test had been performed on bacteriologically proved excreters of typhoid bacilli with a suitable number of controls shown to be non-excreters of the organism. All the 11 papers describe somewhat different methods or use different materials and few of them included a standard Vi serum as a control. The author summarizes the individual results in 9 of these papers and then brings 6 of them into a pool for analysis. He anticipates objections to such a procedure and justifies it on the grounds that these results of tube agglutination tests are of the same order and show that an average of 12·4% of proved typhoid carriers have a Vi titre of less than 1 in 5 in their sera. The probability of a Vi reactor being a typhoid carrier has been calculated from the analysis of the so-called sensitivity and specificity of the test, and the author concludes that the Vi test is not a reliable test for screening populations for typhoid carriers.

[Whether the author's conclusions are correct or not, there are objections to the acceptance of the material he uses for his analyses. For the most part the so-called quantitative results he makes use of are not comparable owing to the variety of the methods and reagents employed and the absence of any common standard control serum even in the few cases where any attempt at control was mentioned. If however the author feels that the test is not suitable for the wide screening of populations because it cannot be relied upon to reveal 100% of the typhoid carriers examined, without the occurrence of false positives, few would disagree with him on the evidence at present available. There can be no doubt about the correctness of the original observations of FELIX *et al.* [*J. Hygiene,* 1935, v. 35, 421; this *Bulletin,* 1936, v. 11, (71)] but no one was more fully aware of the difficulties of the test than he. Felix frequently tried out methods for increasing the sensitivity of the test without loss of specificity, but up to the time of his death he was not satisfied that the Vi-haemagglutination test was sufficiently specific. This latter test has gained favour with many workers in recent years: SCHUBERT *et al.* [*ibid.,* 1959, v. 34, 1091], employing the Standard Tube method, with a haemagglutination and also a slide agglutination technique in series under strictly controlled conditions, reported that the combined results of the three tests gave a very high degree of specificity and that less than 1% of the sera from known typhoid carriers failed to show Vi antibody.]

H. J. Bensted

CHOMICZEWSKI, J. **The Influence of the Antibiotics on the Factors determining Phage-Type Specificity in *Salmonella typhosa*.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 7, 311–15.

16 strains of *Salmonella typhi* were grown in the presence of varying concentrations of 5 antibiotics in fluid and solid media, and the strains were then tested to see

if they had changed their sensitivity to Vi typing phages. Although most resistant strains showed changes in colonial morphology, no differences in phage type were observed among strains grown in the presence of penicillin or chloramphenicol. 1 strain resistant to streptomycin lost its sensitivity to phage 26 and acquired sensitivity to phage 25, and cultures partially resistant to chlortetracycline or to oxytetracycline derived from another strain showed reduced sensitivity to phage C3. None of the strains had lost its lysogenic phage after antibiotic treatment and all retained the Vi antigen.

Janice Taverne

SACQUET, E. Contribution à l'étude de la sensibilité de diverses lignées de souris à l'inoculation de *Salmonella typhi*. [**Studies on the Susceptibility of Different Strains of Mice to *Salmonella typhi* Experimental Infection**] *Ann. Inst. Pasteur.* 1960, June, v. 98, No. 6, 880–86, 2 figs.

There has been a considerable amount of criticism of the intraperitoneal method for the assessment of the LD50 in mice of strains of typhoid bacilli. If simple saline suspensions of typhoid bacilli are employed very large doses of organisms—the minimum being in the region of 40 x 10^6 bacilli—are required to kill mice and the use of mucin preparations to suspend the bacteria is not favoured by many workers. The intracerebral route was considered by LANDY *et al.* [this *Bulletin*, 1957, v. 32, 795 *bis*] to offer many advantages and these workers showed that with a certain strain of mouse the mouse-virulence of the classical *Salmonella typhi*, Ty2, as assessed by the cerebral route of injection was in the region of 200 bacteria.

The present paper is concerned with a re-examination of the problem with a number of different strains of mice. The Ty2 strain of the typhoid bacillus was used throughout these tests. The author confirms that the intracerebral route offers a more delicate method of differentiating the susceptibility of the various strains of mice than the intraperitoneal method, but did not find that the mouse-strain BALB/C had the very high sensitivity that Landy and his colleagues had noted.

H. J. Bensted

EDSALL, G., GAINES, S., LANDY, M., TIGERTT, W. D., SPRINZ, H., TRAPANI, R. J., MANDEL, A. D. & BENENSON, A. S. **Studies on Infection and Immunity in Experimental Typhoid Fever. I. Typhoid Fever in Chimpanzees orally infected with *Salmonella typhosa*.** *J. Exper Med.* 1960, July 1, v. 112, No. 1, 143–66, 4 text figs. & 3 figs. on 2 pls. [44 refs.]

This paper sets out the detailed findings on the establishment of and course of typhoid fever in the chimpanzee. Subsequent papers will be concerned with immunity to typhoid fever and a more complete description of the pathological picture as seen in this animal. These important studies were commenced some years ago and several preliminary reports by members of the group of workers have already appeared (*Fed. Proc.*, 1954, v. 13, 490; *Bull. New York Acad. Med.*, 1955, v. 31, 776; *Fed. Proc.*, 1956, v. 15, 614; *Bact. Proc.*, 1957, v. 10, 79; *ibid.*, 1958, v. 11, 77). The present paper is the first of the series of complete or detailed reports from this group of workers on their studies.

GRÜNBAUM (*Brit. Med. J.*, 1904, v. i, 817) was among the earliest of the investigators to feed typhoid bacilli to chimpanzees and to reproduce some of the characters of typhoid fever in these animals, including a rising Widal reaction. It will be recalled that Grünbaum (*Lancet*, 1896, v. ii, 806, 1747) was the first to observe specific agglutinins in the blood of patients suffering from typhoid fever, although his observations were not published until after the paper by WIDAL (*Bull. Mém. Soc. Hôp., Paris*, 1896, v. 6, 26). Grünbaum's work was extended by METCHNIKOFF and BESREDKA (*Ann. Inst. Pasteur*, 1911, v. 25, 193, 865) who obtained results of the same order. Their experiments also showed that while the higher apes could suffer from enteric fever after oral infection with typhoid bacilli other species were not suitable for such experiments.

Since that time, in spite of the frequent attempts to produce experimental infections in laboratory animals, mainly guineapigs and mice, there has been no satisfactory evidence to show that a true infection could be induced in these small laboratory animals whether by oral or intraperitoneal inoculation. The recent experiments of GERICHTER (*J. Hygiene*, 1960, v. 58, 307) on the so-called oral infection of mice with typhoid bacilli are of considerable interest with regard to the path by which the organism reaches the blood-stream, the liver and the spleen, but since there was no evidence of multiplication of typhoid bacilli in the organs the picture obtained cannot be regarded as a reflection of the events of typhoid fever in man.

The present study is concerned with the clinical and pathological picture in young Congo and West African chimpanzees of both sexes, ranging in weight from 10 to 30 lbs., after receiving an oral challenge of *Salmonella typhi*—either strain Ty2 or the strain 2593, of different phage type to Ty2, but otherwise with similar properties—given in the form of a measured dose injected into an unbroken banana. After an incubation period of 4–7 days the clinical spectrum of disease ranged from a moderately severe typhoid-like fever of short duration to an afebrile infection, with or without bacteraemia (but invariably with an antibody response), and occasionally leading to the development of a persisting biliary infection and a carrier state. The pathological picture, both naked-eye and histological, was indistinguishable essentially from that seen in mild typhoid fever in man. Severe or complicated forms of typhoid fever were not seen in the chimpanzee. The dose of typhoid bacilli, even with the highly mouse-virulent strain Ty2, required to produce the clinical disease in the chimpanzee was very much larger than would have been expected—not less than 1,000 million viable bacilli.

[Judged by what we believe to be the order of the dose necessary to produce typhoid fever in man this is very large. It must not be forgotten, however, that the chimpanzees used in the experiments weighed less than 30 lbs. An adult chimpanzee, even a young adult, will weigh 6 stone or more, and these animals must

therefore be regarded as equivalent, on weight at any rate, to quite young children. Typhoid fever is relatively uncommon in young children; the degree of exposure to risk may of course generally be less than with adults but this is uncertain. When children do develop the disease severe constitutional disturbances are less frequently seen and in the reviewer's experience heavy bacteraemias may be found in children without any evidence of the typhoid state or any other severe signs. If the tissue reactions of man and the chimpanzee to the typhoid bacillus are comparable, and this report indicates that they are, then it may well be that the large dose necessary to produce typhoid fever in baby chimpanzees is merely a reflection of the same conditions obtaining in human babies or very young children.

The difficulties of using full-grown chimpanzees in experiments of this sort are fully appreciated, but it would be most valuable if it could be shown that the baby chimpanzee was more resistant to infection with typhoid fever than the adult animal, as is believed to be the case in man; a belief which still requires scientific evidence for its support.

This is a most important paper and further papers in the series will be awaited with interest.] *H. J. Bensted*

Staub, Anne M. Bases chimiques de la spécificité immunologique des antigènes des Salmonella. **[Chemical Basis of Immunological Specificity of *Salmonella* Antigens]** *Ann. Inst. Pasteur.* 1960, June, v. 98, No. 6, 814–28, 2 figs. on pl. & 2 text figs. [31 refs.]

This is a difficult article to abstract because it does not describe a single piece of research, but gives the substance of a lecture by Mlle. Staub to La Société Francaise de Microbiologie in which she describes her work over the years and that of her colleagues on the immunochemistry of the salmonella O-antigenic factors —particularly the O factors 1, 9 and 12. (See Pon and Staub, *Bull. Soc. Chemie Biol.*, 1952, v. 34, 1132, this *Bulletin*, 1953, v. 28, (466); *ibid.*, 1955, v. 30, 355; Staub *et al.*, *ibid.*, 1956, v. 31, (1149); 1959, v. 34, 669; 1960, v. 35, 1041; *C.R. Acad. Sci.*, 1956, v. 243, 1460; *Bull. Soc. Chemie Biol.*, 1957, v. 39, Sup. I, 65, etc. These papers appear to contain practically all the information presented by Mlle. Staub in her lecture.)

H. J. Bensted

Ter-Karapetyan, A. S. **Antigenic and Immunogenic Properties of IEM Gamaleya Polyvalent Vaccine.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 8, 61–6. [15 refs.] [Translated from Russian.]

Although no details are given about the constitution of the IEM Gamaleya polyvalent vaccine it would appear from the context of the paper to be a typhoid-paratyphoid-dysentery vaccine. The assessment of the antigenic and immunogenic properties was based on a comparison of agglutinin levels of typhoid, paratyphoid B, Flexner and Sonne antibodies before and after the administration of the vaccine to 28 persons and an estimation of the protection afforded as displayed by passive protection tests in mice. It is stated by the author that the protective power of the sera of immunized persons, up to the 4th month after vaccination, showed considerable increases as compared with the pre-vaccination sera. The agglutinin response to the typhoid, paratyphoid and the Flexner was satisfactory, but Sonne agglutinins were not found in any of the sera of vaccinated persons. The vaccine apparently did not induce the development of precipitins or complement-fixing antibodies. *H. J. Bensted*

Tanaka, N., Nishimura, T. & Yoshiyuki, T. **Histochemical Studies on Experimental Typhoid by means of Fluorescein-Labeled Antibody. I. Cellular Localization of the Antigens of *Salmonella enteritidis* after Injection of the Killed Vaccines.** *Japanese J. Microbiol.* 1959, July, v. 3, No. 3, 267–76, 6 figs. on pl. [14 refs.]

The authors studied the localization of the antigens of *Salmonella enteritidis*, after intravenous and intraperitoneal injections into mice of heat-killed and chrome vaccines, by means of fluorescent antibody. In the liver the antigens filled the cytoplasm of the Kupffer cells and the cytoplasm of the monocytes and the granulocytes infiltrating the sinusoids. When the granuloma formed the antigens could be demonstrated in the cytoplasm of the epithelioid cells, but the amount of antigen in the granulomata varied considerably. In the spleen the antigens were localized in the cytoplasm of the large round mononuclear reticular cells of the pulp in the case of the chrome vaccine whereas with the heat-killed vaccine the antigen tended to accumulate in cells lining the lymphoid follicles. The soluble antigens were taken up by the round cells of the entire red pulp.

H. J. Bensted

Daikos, G. K., Papadoyanakis, N. & Athanasiadou, Maria. Empfindlichkeit von Salmonellen gegenüber Synnematin B und anderen Antibiotica. **[The Sensitivity of Salmonellae to Synnematin B and other Antibiotics]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 6, 522–6. 1 fig.

These authors from Athens determined the minimum inhibitory concentration of synnematin B and of some other antibiotics for 18 strains of *Salmonella typhi* and 1 and 9 strains respectively of *Salmonella paratyphi A* and *B*, all isolated from blood cultures. The results are presented as graphs showing percentages of total strains inhibited by different concentrations. The order of decreasing activity was chlortetracycline, oxytetracycline, chloramphenicol, tetracycline, tetracycline + oleandomycin, synnematin B, streptomycin. All strains were inhibited by synnematin B in a concentration of 10 μgm./ml., and 22 and 2 respectively by 5 and 2·5 μgm./ml., but none by any lower concentration. As the authors remark, other investigators have found the activity of this antibiotic to be greater against these organisms [this *Bulletin*, 1955, v. 30, 630, 956]. Similar tests were done with strains of *Escherichia, Klebsiella, Pseudomonas* and *Proteus* spp.: results are given only

as total numbers of all species together inhibited by different concentrations, and synnematin B thus appears to be the least active of all the antibiotics, but it is mentioned that *Proteus* spp. were more sensitive to it than the other organisms. [The authors do not say whence they obtained synnematin B, or what was its degree of purity. The use of impure material appears the most likely explanation of discrepancies between their findings and those of other workers.]

L. P. Garrod

PAPAVASSILIOU, J. Colicinogénie et sensibilité aux colicines des *Salmonella typhimurium* isolées au Congo belge. **[Colicinogenicity and Sensitivity to Colicines of *Salmonella typhimurium* Isolated in the Belgian Congo]** *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 369–72.

The English summary appended to the paper is as follows:—

"Of 71 strains of *Salm. typhimurium* isolated in the Belgian Congo 3 were colicinogenic. 2 strains produced colicine I, and 1 colicine K. Tests of the sensitivity of 40 strains of the organism showed that all were resistant to 13 colicines (V, B, E, I, K, S_3+I, D, S_4, F, A, J+I, C and X). These results show that neither colicinogenicity nor colicine typing are of any practical value epidemiologically in the Belgian Congo."

VASSILIADIS, P. Les Salmonellae du Congo belge (Huitième Rapport). **[Salmonellae of the Belgian Congo]** *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 423–8. [22 refs.]

The English summary appended to the paper is as follows:—

"In this report the author presents the new data on Salmonella of the Belgian Congo and Ruanda-Urundi from the 1st March 1959 until the 1st March 1960.

"Twelve serotypes are added to the 148 previously described in these countries. Among them *S. gombe* (6,7 : d : e,n,z15) and *S. ruki* (1,4,5,12 : y : e,n,x) are new species. The frequency of the various serotypes isolated and localisations in man are briefly mentioned."

BELAIA, I. A. **A Study of the Biological Properties of Dysentery Strains tested in Chick Embryos and on the Model of Experimental Dysenteric Keratoconjunctivitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 12, 48–51. [11 refs.] [Translated from Russian.]

"(1) Freshly isolated strains of *Shigella* were highly virulent in tests in chick embryos.

"(2) There was a complete correlation between the virulence of the strains as tested in embryos and by the keratoconjunctivitis test. Those strains in which 1 Dcl for the embryo was 2–200 organisms produced infection in the guinea-pig eye.

"(3) A high virulence as shown in tests in chick embryos is evidence of the antigenic completeness of the strain, and in the selection of strains for the production of vaccine it must be taken into account, along with the keratoconjunctivitis test and the other known tests."

FOLSOME, C. E. **Effects of 5-Bromodesoxyuridine upon Gene Recombination in *Escherichia coli* K-12.** *Genetics.* 1960, Aug., v. 45, No. 8, 1111–22, 2 figs. [23 refs.]

FRISCH, D. M. & VISSER, D. W. **Synthesis of Protein and DNA in *Escherichia coli* treated with 5-Bromodeoxyuridine.** *Biochim. et Biophys. Acta.* 1960, Oct. 7, v. 43, No. 3, 546–8, 4 figs. [12 refs.]

SAHAB, K. **Further Studies on *Escherichia coli* with B Antigens using the Stained Capsular Reaction.** *J. Bacteriology.* 1960, Aug., v. 80, No. 2, 212–17.

CLOSON, J. & BETZ-BAREAU, M. Dégradation de la 3:5:3'-triiodo-L-thyronine par *Escherichia coli.* **[Degradation of 3:5:3'-triiodo-L-thyronine by *Escherichia coli*]** *C.R. Soc. Biol.* 1960, v. 154, No. 4, 844–8, 1 fig.

GILLIES, N. E. & ALPER, T. **The Nucleic Acid Content of *Escherichia coli* Strains B and B/R.** *Biochim. et Biophys. Acta.* 1960, Sept. 23, v. 43, No. 2, 182–7. [22 refs.]

KUDLAI, D. G. & KANTARBAEVA, Z. K. **Antagonism as a Criterion for the Determination of Species in Micro-Organisms.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 8, 40–46, 4 figs. [Translated from Russian.]

Organisms related through a common origin are mostly indifferent to each other in culture. For instance when two strains of *Escherichia coli* are grown close to each other on the same culture medium, neither influences the growth of the other in the majority of cases, but in some instances a synergistic effect may be noted and in others an antagonistic effect. In one series of 86 strains of *E. coli* the authors found that within the species the most frequent type of interrelation was indifference (65·1%). Synergism occurred in 29·1% and antagonism in 5·%. With *E. coli* and typhoid bacilli the antagonistic effect was found to be more frequent and by selection of strains and special techniques reproducible results can be obtained.

[During recent years many observations have been recorded on the antagonistic effect of one bacterial species on another, or between different strains of the same species. Occasionally an antibiotic substance has been separated but mostly the observations have established no more than a pattern of antagonisms. The authors make no reference to the colicines, the large-particle but diffusible "antibiotics" of *E. coli* and other intestinal bacteria, nevertheless the antagonism they

describe, had they used the more elegant layer-technique of GRATIA *et al.*, [this *Bulletin*, 1950, v. 25, 950] would probably be shown to be due to a diffusable substance.] *H. J. Bensted*

BLACKWELL, J. T., Jr. & MCVEIGH, Ilda. **Growth of Streptomycin-Susceptible and Streptomycin-Resistant Strains of *Escherichia coli*.** *Antibiotics & Chemotherapy*. New York. 1960, Aug., v. 10, No. 8, 495–502, 2 figs.

These experiments were made with a strain of *Escherichia coli* sensitive to dihydrostreptomycin and variants of the same strain resistant to it. In both a complex and a minimal synthetic medium the resistant variants grew more slowly: in the latter medium they also showed a very prolonged lag. Growth in either medium from an approximately equal inoculum of sensitive and resistant culture was followed by ever more rapid overgrowth of the resistant cells than was to be expected on the basis of the previous findings, the resistant organisms sometimes becoming irrecoverable (by plating on antibiotic-containing medium) after 48 hours. *L. P. Garrod*

MOLDAVE, K. **The Incorporation of Radiocarbon from ATP and Amino Acid into Nucleic Acids of *Escherichia coli*.** *Biochim. et Biophys. Acta.* 1960, Sept. 23, v. 43, No. 2, 188–96, 3 figs. [29 refs.]

WOODSIDE, E. E., GOUCHER, C. R. & KOCHOLATY, W. **Postirradiation Responses of Ultraviolet irradiated *Escherichia coli*.** *J. Bacteriology*. 1960, Aug., v. 80, No. 2, 252–8, 6 figs. [23 refs.]

KADA, T., BRUN, E. & MARCOVICH, H. Comparaison de l'induction de mutants prototrophes par les rayons X et U.V. chez *Escherichia coli* B/r Try−. **[Comparison of Prototroph Mutants induced by X and U.V. Rays in *E. coli* B/r Try−]** *Ann. Inst. Pasteur*. 1960, Oct., v. 99, No. 4, 547–66, 13 figs.

PARNAS, J., with the assistance of W. BULIKOWSKI, T. BIELUGA & L. SZECHTER. État actuel de nos recherches sur les phages anti-*Brucella*. **[The Present State of Research on Brucella Phages]** *Arch. Inst. Pasteur de Tunis*. 1960, June, v. 37, No. 2, 215–25. [13 refs.]

The author has isolated a number of brucella phages himself and has also received several from Madame DROZEWKINA and other workers in the U.S.S.R. In this he reports the testing of these phages against a large collection of *Brucella* strains from various sources. The results are not startlingly different from those previously reported [this *Bulletin*, 1958, v. 33, 1180; 1959, v. 34, 684] where the activity of the phages was most marked with typical strains of *Br. abortus* and least marked with typical strains of *Br. melitensis*. But the phage patterns that have so far emerged from the investigations are not sufficiently distinct to indicate how far the range of activity of the present phages can be utilized for epidemiological purposes. *H. J. Bensted*

DESSI, P., GIANNI, A. M., PASINI, G. & GRECO, M. Aminoacidi liberi e delle proteine di struttura di *Brucella melitensis* resistente alla terramicina. **[Free Amino-Acids and Amino-Acids of Structural Proteins in *Brucella melitensis* Resistant to Oxytetracycline]** *Giorn. di Microbiol.* Naples. 1960, Apr.–June, v. 8, No. 2, 122–8, 1 pl. [21 refs.] English summary.

PARNAS, J., ZWOLSKI, W., BURDZY, K. & KOSLAK, A. **Zoological, Entomological and Microbiological Studies in Natural Foci of Anthropozoonozes. *Brucella brucei* into *Hoplopleura acanthopus* Burm.** *Arch. Inst. Pasteur de Tunis*. 1960, June, v. 37, No. 2, 195–213, 3 figs. [26 refs.]

The first part of this paper is concerned with the trapping and examination of mammals and birds in the Lublin area of Poland and the identification of their ectoparasites—ticks, fleas and lice. The object of this investigation was to determine whether any of these ectoparasites carried, or were naturally infected with, leptospires or brucellae. All the results were negative, and moreover there was no evidence, from feeding experiments, that any of the ticks, fleas or lice tested could carry a leptospiral infection. On the other hand with brucella infections it was shown that the louse, *Hoplopleura acanthopus*, could carry the organism after feeding on an artificially infected *Microtus arvalis*, a small field rodent. *Hoplopleura acanthopus* is a relatively large species of louse which is fairly common in Europe and may be found on a number of field rodents. [The observation is of interest but its importance is difficult to determine.] *H. J. Bensted*

SULITZEANU, D. **The Fate of Killed, Radioiodinated *Brucella abortus* injected into Mice.** *J. Immunology*. 1959, Apr., v. 82, No. 4, 304–12, 1 fig. [18 refs.]

"Following intraperitoneal injection of radio-iodinated, acetone killed *Brucella abortus*, the spleens and livers of normal mice collected a higher amount of radioactivity and the mesenteric lymph glands a lower amount, than the corresponding organs of immune animals. The distribution of the label was similar, whether the mice had been actively immunized with a living or killed vaccine or passively immunized with mouse or rabbit anti-Brucella serum. There was a good correlation between the immunizing dose and the radioactivity in the mesenteric glands.

"Labeled bacteria sensitized with antibody behaved in the normal animal in a manner identical to that of the nonsensitized bacteria in the immune animal.

"The radioactivity found in the organs was shown to be attached to heavy particles retaining their antigenic properties, presumably intact bacteria.

"A considerable proportion of the injected brucellae was destroyed and the breakdown products excreted during the first 6 hr after inoculation."

SULITZEANU, D., BDOLACH, A. & SPERLING, O. **The Fate of Killed, Radioiodinated *Brucella abortus* injected into Mice. II. Mechanism Determining the Distribution of the Injected Bacteria.** *J. Immunology*. 1960, June, v. 84, No. 6, 551–61, 3 figs. [19 refs.]

Radio-iodinated *Brucella abortus* injected intraperitoneally into mice are partly taken up by the peritoneal phagocytes and the remainder leave the abdominal cavity by the lymphatic system and quickly reach the blood stream which carries them to the liver and the spleen, where they are trapped. Of those phagocytosed in the peritoneal cavity some are quickly destroyed but a significant proportion of the engulfed bacteria migrate to the mesenteric lymph glands. The proportion of radio-iodinated brucellae reaching the mesenteric glands is greatly increased by conditions favouring phagocytosis, such as a peritoneal exudate, stimulation of the reticulo-endothelial system or the presence of brucella antibodies. Thus the radio-activity in the mesenteric glands will be increased at the expense of the radio-activity in the liver and spleen. *H. J. Bensted*

BOUVIER, G. Sensibilité de *Brucella abortus* au pH et à certaines solutions faiblement bactéricides. Nouvelle technique d'isolement des *Brucella* dans du matériel fortement souillé (arrière-faix de bovins). **[Sensitivity of *Brucella abortus* to pH and to certain Weakly Bactericidal Solutions]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 202–10, 4 figs.

In studying the contagious abortion of cattle the author was successful in isolating *Brucella abortus* from dead foetuses and the foetal membranes pre-treated with slaked lime to kill off contaminating organisms. Preliminary experiments having shown that *Br. abortus* could withstand exposure to low *p*H (20% solutions of calcium superphosphate = *p*H 2·7) and also exposure to high *p*H (1–5% slaked lime = *p*H 11·5), extremes which were bactericidal to the organisms usually contaminating dead foetuses and the foetal membranes in cases of contagious abortion, a routine isolation technique was evolved.

Fragments of placenta or other suitable materials were first shaken vigorously in a solution of 1, 2 or 5% slaked lime for 15 minutes; after high speed centrifugation and thorough washing in normal saline, with three changes, the specimens are transferred to special *Brucella* culture media, some containing crystal violet and some without the dye, and incubated at 37°C. in an atmosphere of CO_2. Out of 50 specimens thus examined *Br. abortus* was isolated from 49.

The author agrees that the alkali treatment probably destroys many brucellae in effectively dealing with all the contaminating organisms in the specimens including *Proteus*. Since, however, the placenta is usually very heavily infected with *Br. abortus* a sufficient number survive the treatment so that there is little difficulty in isolating them in pure culture. *H. J. Bensted*

HUZIWARA, T. & HYÔDÔ, S. Sur des substances antigéniques de *Pasteurella tularensis*. Immunisation de souris par des antigènes extraits. **[Antigenic Substances of *Brucella tularensis*. Immunization of Mice by Extracted Antigens]** *C.R. Soc. Biol.* 1960, v. 154, No. 4, 877–80.

HUZIWARA, T. & SAWANO, M. Sur des antigènes polyosidiques de *Pasteurella tularensis*. Identification des sucres constitutifs. **[Polysaccharide Antigens of *Brucella tularensis*. Identification of Component Sugars]** *C.R. Soc. Biol.* 1960, v. 154, No. 4, 881–3.

BÜRKI, F. Zum Nachweis von Leptospiren mittels des Goldhamster-Tierversuchs. **[Use of Syrian Hamster to demonstrate Presence of Leptospires]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 211–22. [19 refs.]

Seven strains of leptospires were used in this investigation. 0·5 ml. of 14-day cultures in Korthof medium were injected intraperitoneally and the heart blood of the hamster subcultured to the same medium after 2 or more days and from other animals kidney juice was examined for leptospires after 21 days. At the same time the presence of antibodies was sought in the blood serum.

100% of positive results were obtained with *L. pomona*, *L. canicola* and *L. icterohaemorrhagiae*, *L. grippo-typhosa* and *L. hyos*, although the speed of growth varied considerably among these. *L. sejrö K* and *L. sejrö* did not readily infect the hamster.

Although the leptospires were not recovered from the kidneys in any of these infections, the appearance of antibodies in the serum at the end of 21 days was usual.

There was an interesting contrast between *L. canicola* and *L. pomona*. The former could be got to grow in K medium even from a 10^{-6} dilution of a previous culture, but could not be recovered from the hamster if the inoculum was diluted 10^{-2} and the rodents always survived beyond 21 days.

With *L. pomona* subculture failed at a dilution of 10^{-2} but even diluted 10^{-4} it still killed the hamster with an acute generalized infection within 10 days.

J. W. McLeod

BABUDIERI, B. Die Zellstruktur und die Serologie der Leptospiren. **[Cell Structure and Serology of Leptospires]** *Ergebn. Mikrobiol. Immunitätsf.* 1960, v. 33, 259–306, 5 figs. [Numerous refs.]

A lengthy critical review of the literature bearing on leptospires is presented. The work includes the most recent work on morphology of the organisms and classification by immunological methods.

The more recent observations on leptospiral morphology based on the findings with the electron microscope on whole organisms and sections are reviewed. The author concludes that the only clearly-established features are a single axial filament, the protoplasm wound around it and a defined limiting membrane containing both. The evidence for nuclei, spores and flagella is considered inadequate. They are classified in the author's fifth family, *i.e.* spirochaetaceae without septum, provided with an axial filament and devoid of volutin granules.

Serological

The lysis reaction in leptospires is a peculiar phenomenon in bacteriology since it occurs in absence of complement; but the actuality of lysis has been queried, it being suggested that the granules developing in "lysed" cultures can, by suitable disintegration, be made to yield leptospires.

The author deals at length with phenomena of cross- and para-agglutinations and the different extent to which they are observed in the sera of different animals. They may be asymmetrical, *e.g.* human antiserum to *L. pomona* agglutinates *L. icterohaemorrhagiae*, but the reverse does not hold.

Precipitin observations suggest affinity between leptospires, shigellae and even *Trypanosoma cruzi*.

Many other reactions of immunity which have been adopted with a view to getting better methods of grouping the different pathogenic strains are discussed. Such are the flocculation, thrombocytobarin, protection of experimentally infected animals, the coagulation reaction of CARLINFANTI, haemagglutination, allergy and complement fixation. Among these it is suggested that the animal protection test is occasionally valuable in type differentiation. Complement fixation is less type specific than agglutination but as the presence of the antibodies in the blood is of much shorter duration it may be valuable in picking up recent cases in an area where leptospiral infection is common, and there is a considerable part of the population carrying agglutinins due to infection at a remote date.

The effective antigens appear to be mainly polysaccharides and protein antigens have not been demonstrated.

The rather shaky classification at present adopted depends mainly on differentiation by type specific agglutinins as determined by methods of agglutinin absorption, and distinguishes 18 groups, many of which contain several sero-types and sub-types. *J. W. McLeod*

KOLOCHINE-ERBER, Berthe & MAILLOUX, M. Difficultés du diagnostic sérologique de certaines leptospiroses (*L. grippo-typhosa* et *L. australis*). **[Difficulties in the Sero-Diagnosis of certain Leptospiroses (*L. grippo-typhosa* and *L. australis*)]** *Ann. Inst. Pasteur.* 1960, May, v. 98, No. 5, 629–41. [25 refs.]

Agglutination-lysis tests in leptospirosis often clearly indicate the identity of the infecting serotype; but tests may be difficult to interpret when the serum reacts with more than one serotype. The authors discuss, with examples from their own case records, various difficulties which may occur in the differential diagnosis of infections with *Leptospira grippotyphosa* and *L. australis A*, but they note that similar problems arise with other serotypes.

The clinical pictures of leptospirosis caused by *L. grippotyphosa* and *L. australis* have many common features of which the most noteworthy are the frequency of headache with meningeal symptoms and the rarity of jaundice. Moreover, serological tests repeated at intervals of about 4 weeks often reveal the occurrence of antigenic factors (co-agglutinins) common to both serotypes.

Serological reactions (agglutination-lysis) may be subdivided into 4 groups. (1) Agglutination and lysis occur with only one serotype, or to a markedly higher titre with one; therefore the diagnosis is obvious. (2) In spite of the presence of co-agglutinins [cross-agglutination], a diagnosis can be made from a series of tests. For example, the agglutination titre of one serotype rises higher and more rapidly; or the rise in titre of one serotype is maintained while the titre of the other declines; or the titre of one rises from zero to a high level while that of the other remains at a comparatively low level throughout. (3) Interpretation remains difficult in spite of serial testing as happens when the titres of the two serotypes rise and fall more or less in parallel. In such cases, continued serial testing may reveal a significant difference in the pattern of the titres [or the diagnosis may be made from agglutinin-absorption tests (PATHY, this *Bulletin*, 1960, v. 35, 1007.] (4) The serological results continue to be equivocal, but isolation of a strain of leptospires from the patient clinches the diagnosis.

The authors support the view of ROTHSTEIN and HIATT [*ibid.*, 1957, v. 32, 502] and of SCHNEIDER [*ibid.*, 1954, v. 29, 1262; 1956, v. 31, 583] that leptospires contain at least 2 somatic antigens: one genus-specific, the other type-specific. A genus-specific agglutinin (co-agglutinin) could explain the phenomenon of cross-agglutination so often seen in tests on sera obtained in the second and third weeks of leptospiral infections. The type-specific agglutinin appears later [and tends to persist longer]. Sometimes the identity of a strain isolated from a human patient or an animal seems not to conform with expectations based on the serological reactions obtained; the reasons for this apparent paradox are not yet clear.

The occurrence of common antigenic components among leptospires (as among other organisms) has led to the concept of serogroups within the genus, each serogroup being comprised of a number of distinct serotypes. The authors note, however, that certain strains occur which have properties common to several serogroups. *L. H. Turner*

FÜZI, M. & CSÓKA, R. Über die Einordnung der *Leptospira leeds* in das System. **[Classification of *Leptospira leeds* into the System]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 222–8. [18 refs.]

This paper deals with a subculture of the strain observed by CZEKALOWSKI and HORNE [*Brit. Med. J.*, 1951, ii, 879; see also this *Bulletin*, 1954, v. 29, 880] in a case of acute bacterial cystitis 9 years ago, of which the subculture had been obtained from the collection of Professor Babudieri of Rome. The strain originally observed

by Czekalowski and his collaborators had been described as a coarsely growing form which in its cultural reactions corresponded most nearly to the saprophytic leptospira.

The authors have checked the finding by more extensive observations including the testing of antisera to this organism with suspensions of a very large number of the known pathogenic leptospires and two strains of saprophytic water leptospires: and have also used the tests of resistance to copper salts and digestion of yolk of egg in suitable conditions of culture. By both the latter tests the leptospire strain fell into line with the saprophytic water spirochaetes *L. biflexa* Patoc I the *L. biflexa* AM-3. There was not any evidence of antigenic similarity between the Leeds strain and the saprophytic strains from water or any of the pathogenic strains. In brief, the position remains the same as in the earlier paper. The leptospire in question must either have arisen as a contamination at some stage in obtaining the sample of the urine or it represents one of a group of strains of leptospires commensal in the urinary or genital tract which has not yet come under serious investigation. *J. W. McLeod*

SHIRVINSKAIA, A. I. **Study of Type-Specific Immunity in Experimental Leptospirosis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 10, 39–43. [14 refs.] [Translated from Russian.]

It is well known that under certain circumstances serotherapy and seroprophylaxis in leptospirosis are effective. The general opinion is that protective sera tend to be monovalent or serotype-specific. The author notes that little attention has been paid to the study of cross-immunity (intertype immunity) in leptospirosis: the main reason is the lack of laboratory animals highly susceptible to organisms causing benign anicteric leptospirosis.

The degree of protection afforded by each antiserum immune rabbit sera (titres 11,000–20,000) prepared from strains of the following serotypes of *Leptospira*: *icterohaemorrhagiae AB, canicola, poi, bataviae, saxkoebing, hebdomadis, grippotyphosa, pomona,* and *hyos.* Before being used in the experiments, the virulence of these strains was enhanced by 5–8 serial passages in animals [presumably young rabbits] until typical symptoms, and death in 75–90%, resulted. *L. icterohaemorrhagiae* A (Kantarowicz strain) was avirulent and could only be used for protection of serum.

The degree of protection afforded by each antiserum was first determined by titration in animals in which "the dose protecting against infection was found to be 0·1 ml." The hyperimmune monovalent antiserum was injected intramuscularly into young rabbits. "The dose of homologous serum was 0·2 ml. the dose of heterologous serum five times greater, which ensured more rigid experimental conditions. Two hours after injection of the serum all the rabbits received an intraperitoneal injection of 1 ml. of a virulent culture containing not less than 30–40 *Leptospira* per field of vision. The observations on the animals extended over 10–15 days with daily determination of the temperature and weight." 719 animals were used, of which 178 were controls (rabbits not receiving antiserum and also rabbits injected with 1 ml. of normal rabbit serum).

The results showed that while most antisera only protected against the homologous organism, a few gave cross-protection, as follows: *canicola* and *poi* serum against *icterohaemorrhagiae* AB; *hebdomadis* serum against *saxkoebing. L. saxkoebing* serum protected animals from death but not from illness when they were challenged with *L. hebdomadis.* *L. H. Turner*

FUHRMAN, Geraldine J. & FUHRMAN, F. A. **Inhibition of Active Sodium Transport by Cholera Toxin.** [Correspondence.] *Nature.* 1960, Oct. 1, v. 188, 71–2, 1 fig.

MIKHAILOV, I. F. & LI LI. **Detection of *Vibrio comma* on Objects of the External Environment by means of Fluorescent Antisera.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 8, 33–40, 1 fig. [11 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 61.]

BACTERIOPHAGES

BERTANI, G. **On the Interpretation of Boyd's "Multiplicity Effect" in Lysogenization.** *Virology.* New York. 1960, Sept., v. 12, No. 1, 132–6, 1 fig.

KUBINSKI, H. **The Influence of a Substance from *Escherichia coli* B on the Susceptibility of Phage T2 to Potassium Permanganate.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 7, 275–9, 2 figs. [15 refs.]

An extract of *Escherichia coli* B was prepared by boiling a culture scraped from an agar plate into saline, and centrifuging to remove cell debris. T2 phage was incubated at 37°C. with the supernatant fluid, and at intervals samples were mixed with 0.09% potassium permanganate for 15 minutes and titrated. Control suspensions of phage were incubated with broth containing the same amount of protein as the *E. coli* extract. The bacterial extract alone did not reduce the number of infective particles, neither did potassium permanganate added to the broth controls. However, phage which had been incubated with the extract was inactivated by permanganate, and its susceptibility to permanganate varied with the period of incubation with the extract. It reached a maximum after 30 minutes, and returned to normal

after 90 minutes incubation with the extract. In some experiments second and even third cycles of increase and decrease in susceptibility were observed.

The author suggests that the reaction with some substance in the bacterial extract which sensitizes the phage to permanganate, and which takes time, is reversible, and that after maximum sensitivity is reached the sensitized parts decompose. Further cycles are observed when the reaction is repeated with another set of phage particles. Vi antigen extracted from *Salmonella typhi* has also been observed to increase the susceptibility of Vi phage to potassium permanganate [this *Bulletin*, 1959, v. 34, 682]. *Janice Taverne*

KUBINSKI, H. **The Effect of *Escherichia coli* B Substances on the Sensitivity of Phage *T2* to Toxic Agents.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 8, 347–52, 5 figs. [17 refs.]

Incubation of T2 phage for a short time with an extract obtained by boiling *Escherichia coli* B in saline made the phage more sensitive to inactivation by potassium permanganate [see above] but after longer incubation the sensitivity disappeared. It is reported here that incubation with the same extract also rendered the phage more sensitive to inactivation by formaldehyde. But the period required to achieve maximum sensitivity was different for the two substances, although it was unaffected by the concentration of each substance.

The author supposes that the extract acts on the phage tail in some way, perhaps uncovering a protein which is sensitive to these agents. He does not think that in this case formaldehyde acted on nucleic acids because treatment with the extract did not make the phage more sensitive to methylene blue, a substance known to react with nucleic acids. *Janice Taverne*

SEKELY, Lea I. **Mapping Experiments with Bacteriophage T2L.** *Virology*. New York. 1960, Sept., v. 12, No. 1, 118–24, 2 figs. [11 refs.]

"Twelve new mutants of bacteriophage T2L, most of which were induced by 5-bromouracil, are described. The new mutants and four previously isolated mutants have been mapped by two-factor crosses. All these mutants can be placed upon a single linkage structure which corresponds to linkage groups I and II of Hershey and Rotman (1949). In conjunction with the results of Baylor *et al.* (1957), this provides direct evidence for the commonly held assumption that the genetic structure of the T-even phages consists of a single 'chromosome'."

THOMAS, C. A., Jr. & SUSKIND, S. R. **Production of New Antigens in Phage-Infected *Escherichia coli* K12 (λ).** *Virology*. New York. 1960, Sept., v. 12, No. 1, 1–7, 2 figs. [15 refs.]

"Antisera prepared against crude extracts and fractions of *Escherichia coli* K12 (λ) infected with phage T4 have been completely absorbed with extracts of uninfected K12 (λ). These sera no longer give a positive precipitin reaction or agar diffusion test with extracts of uninfected bacteria, but they still react weakly with intact T4 phage and strongly with both disrupted phage and extracts of T4-infected K bacteria. However, these absorbed antisera, after absorption with intact and disrupted phage particles, exhibit positive precipitin and agar diffusion tests only with extracts of infected bacteria. These results suggest that the residual activity in the serum absorbed with extracts of uninfected bacteria and of phage is due to antibodies produced against new antigens, which are present in the infected cell but are not found in purified phage particles."

CALEF, E. & LICCIARDELLO, G. **Recombination Experiments on Prophage Host Relationships.** *Virology*. New York. 1960, Sept., v. 12, No. 1, 81–103, 2 diagrams. [27 refs.]

"Data from crosses between strains of *Escherichia coli* K12 lysogenic for λ prophages suitably marked show three facts that bear on the problem of structural relationships between prophage and host bacterium. A marked increase can be observed in recombination between the prophage markers when one performs a selection for crossovers between alleles of *gal*. This increase permits a test of linearity of prophage markers relative to bacterial markers. The results of the test show that the two structures are linearly assembled. A marker *mi* can be mapped at a position different from the one found by phage crosses. The meaning of this last fact is discussed in relation to the main problem of structural organization."

TING, R. C. Y. **A Curing Effect of Chloramphenicol on Bacteria infected with Bacteriophage.** *Virology*. New York. 1960, Sept., v. 12, No. 1, 68–80. [19 refs.]

"Early addition of chloramphenicol to cells of *Salmonella typhimurium* infected with phage P22 results in curing a large proportion of the infected cells. The curing action is mutant strain specific: it is effective on wild-type phage P22 c^+ and on its virulent mutant c_2, but is much less effective on another virulent mutant c_1. Curing by chloramphenicol does not prevent transduction by the phage P22. The helping function of phage mutant c_2 for the establishment of lysogeny by c_1, and the ability of phage c_2 to contribute genetic markers to c_1 prophage, are not eliminated by chloramphenicol treatment. The frequency of lysogenization by phage P22 c^+ is much lower on a chloramphenicol-resistant mutant of *S. typhimurium* than on the sensitive strain."

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

STEWART, R. B. **Effect of Cortisone on the Growth of Psittacosis Virus in Cultures of L Cells.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 25–9, 3 figs. [13 refs.]

Virus was grown in cultures of mouse fibroblasts and cortisone acetate was added to the concentration of 100 μgm. per ml. of culture fluid, 24 hours before infection, at the time of infection and, in some experiments, at further intervals of 24 hours up to the 72nd hour. Control cultures, omitting cortisone, were invariably set up. Virus was titrated in the culture fluid and in the cells.

No difference was observed in the first 18 hours between the virus titres, either of the cells or fluids, of the cortisone-treated or control cultures. This suggests that cortisone does not affect the virus take-up. By 48 hours the virus content of the culture fluid was less in the cortisone treated system, though similar in the cells both of the cortisone-treated and control cultures. It is suggested that this is due to suppression of virus release by cortisone. Contrary to expectation, when the action of cortisone was continued beyond this time, the production of virus appeared to be stimulated and somewhere between the 26th and 144th hour the virus content of the culture fluid in the cortisone system surpassed that of the controls. Cell counts and microscopy of the cells showed that the cortisone cultures retained a greater number of intact cells for a longer time than the controls, owing possibly to protection of the cells against the cytopathogenic action of the virus. It is suggested that the higher virus titres in the older cortisone-treated cultures are due to their greater content of virus-producing cells.

S. P. Bedson

BOLOTOVSKII, V. M. **Necessary Conditions for the Successful Production of Experimental Infection with Ornithosis Virus Aerosol.** *Problems of Virology.* London. 1959, v. 4, No. 5, 102–6, 2 figs. [Translated from Russian.]

"The following optimal conditions for the reproduction of aerosol infection in white mice with ornithosis virus in the IVK-1 chamber could be established:

"a) The relative humidity of the air should be 85-95 per cent.

"b) The respiratory exposure of the mice (the time during which the mice are in contact with the aerosol) should last about 60 min."

SHARP, D. G. & SMITH, K. O. **Rapid Adsorption of Vaccinia Virus on Tissue Culture Cells by Centrifugal Force.** *Proc. Soc. Exper. Biol. & Med.* 1960, May, v. 104, No. 1, 167–9, 2 figs.

By centrifuging a mixed suspension of susceptible cells (Earle's L-strain) and vaccinia virus, the rate of adsorption of virus to cells was very greatly accelerated. When centrifuged in a swinging bucket rotor at about 8,000 *g*, 60% of the virus was adsorbed in 4½ minutes, compared with a theoretical time of about 45 minutes if the virus and cell mixture were left to its own devices. Exposure to a centrifugal force of 8,000 *g* does not seem to have damaged the capacity of the cells to produce virus.

Colin Kaplan

SMITH, K. O. & SHARP, D. G. **Interaction of Virus with Cells in Tissue Cultures. I. Adsorption on and Growths of Vaccinia Virus in L Cells.** *Virology.* New York. 1960, July, v. 11, No. 3, 519–32, 6 figs. [16 refs.]

Adsorption rates were determined by direct cell and virus counts. The number of virus particles adsorbed per cell increased directly with time of exposure. As the multiplicity of infection increased, disproportionately more virus was adsorbed to the cells. Even the maximum rate observed, however, fell well short of the theoretical rate at which vaccinia virus may be expected to adsorb to cells in suspension.

Experiments on the multiplication of virus showed, in the first 6 hours, a total particle count diminishing very little, while infectivity decreased considerably. From about 6 hours the number of particles increased rapidly until about 36 hours, with infectivity increasing concurrently. There was no indication of lysis of cells and sudden release of virus. The final ratio of particles to infectivity obtained was about 25. Approximately 10% of the virus particles were in the medium free of cells. the particle to infectivity ratio of this virus was about 70.

Cells infected in the log stage of growth produced an average of 2600 virus particles each; cells in lag phase and stationary phase about 900 each. *Colin Kaplan*

SOLOV'EV, V. D. & MASTIUKOVA, I. N. **A Study of the Multiplication of Vaccinia Virus in Tissue Cultures.** *Problems of Virology.* London. 1959, v. 4, No. 4, 85–91, 4 figs. [11 refs.] [Translated from Russian.]

This paper reports the results of an investigation on a heroic scale of the multiplication of vaccinia virus in 52 different tissue culture systems. In addition to the development of infectivity, haemadsorption, haemagglutinin production and morphological changes in the cells were studied. [The results might have been predicted from the findings of many more restricted investigations.]

Colin Kaplan

SHARP, D. G. **Extraction and Counting of Vaccinia Virus Particles from Calf Lymph Vaccine.** *J. Immunology.* 1960, May, v. 84, No. 5, 507–13, 7 figs.

Small samples of two lots of calf lymph smallpox vaccine were extracted with fluorocarbons by shaking in

a cylindrical device. The clarified supernatant fluid was then centrifuged to deposit the extracted virus particles for electron micrographic counting as described previously [this *Bulletin*, 1959, v. 34, 499]. The particle counts were 1·2 and $7{\cdot}1 \times 10^{10}$/ml. respectively. Both passed the potency requirements of the National Institutes of Health.

When the extraction chamber contained a steel ball instead of a glass one, virus particles had completely disappeared after 15 to 30 minutes of agitation. The author thinks that the fluorocarbon may be involved in the apparent destruction of the virus particles.

Colin Kaplan

Bénard, H., Tissier, Marguerite & Galistin, P. Action de certains corticostéroïdes sur le développement de la vaccine dans l'oeuf de poule incubé. **[Effect of Certain Corticosteroids on the Development of Vaccinia Virus in Chick Embryos]** *C.R. Soc. Biol.* 1960, v. 154, No. 2, 259–62.

Chick embryos were treated with corticosteroids by chorioallantoic inoculation on the 11th incubation day and 1½ hours later vaccinia virus was added. Controls were inoculated with phosphate buffer instead of corticosteroids. After 48 hours' incubation pocks were counted on the chorioallantoic membranes. Neither cortisone acetate nor dexamethasone acetate had any statistically significant influence on pock count. Dexamethasone phosphate, however, almost completely suppressed pock formation when a 1 in 10 dilution was used. Dilutions of 1 in 1,000 and, to a less extent, 1 in 10,000 were associated with an apparently favourable effect on the development of pocks. [The authors give no indication of the concentrations of the steroid solutions from which they prepared the dilutions used in their experiments. The significance of their observations cannot, therefore, be readily assessed.] *Colin Kaplan*

Postlethwaite, R. & Maitland, H. B. **The Eclipse Phase of Vaccinia Virus growing in Chick Embryo Cell Monolayers and Some Technical Procedures which Affect its Demonstration.** *J. Hygiene.* 1960, June, v. 58, No. 2, 133–45.

The authors showed that after infection of chick embryo cell monolayers with ultrasonically treated virus the amount of infectious virus which could be recovered decreased for about 5 or 6 hours and then increased. They also showed that up to 10½ hours after infection of monolayers with an inoculum treated by ultrasonic vibration, whole cells gave higher plaque and pock counts than comparable cells which had been disintegrated. They regard these findings as reasonable evidence for the occurrence of an eclipse phase in the replication of vaccinia virus.

The authors noted that inoculum not treated with ultrasonic vibration did not show a rapid loss of infectivity after mixing with cells, whereas ultrasonically treated virus did. They were unable to offer an explanation for this. *Colin Kaplan*

Kunert, H. & Wolff, I. Vergleichende Untersuchungen über die Virulenz der Vakzine-Virusstämme Berlin und Bern. **[Comparative Investigations of the Virulence of the Berlin and Bern Strains of Vaccinia Virus]** *Arch. f. Hyg. u. Bakt.* 1960, Feb., v. 144, No. 1, 37–47, 2 figs.

A comparison has been made of the Berlin and Bern strains of vaccinia virus in laboratory experiments. The Berlin strain is derived from a mixture of 3 strains, 1 of which is an attenuated strain of variola, and has been passaged in several animal species. The Bern strain has been passaged in calves since 1898. Vaccine pulp was prepared from the 2 strains under identical conditions; the titres were determined by 4 different methods, and remained reasonably constant during storage for 14 months at 4°C. The Berlin strain produced much more necrosis than the Bern strain when inoculated on the rabbit skin, and some animals developed a general reaction with fever, loss of weight, rhinitis, conjunctivitis and diarrhoea which was not seen with the Bern strain. Since 1959 the Bern strain has been used for vaccine production in Berlin, and no complications have been observed in 6,000 persons vaccinated with it.

D. J. Bauer

Kaplan, C. **Reactivation of Vaccinia Virus inactivated by Mercury.** [Correspondence.] *Nature.* 1959, Oct. 3, v. 184, Suppl. No. 14, 1074.

Vaccinia virus was completely inactivated by incubation with 10^{-4} M mercuric chloride at 37°C. for 60 minutes, the infectivity as determined by pock counting falling to zero, as compared with $0{\cdot}8 \times 10^7$ infectious units per ml. in a control preparation incubated with 0·05M cysteine. When the inactivated virus was incubated at 37°C. for 30 minutes with cysteine in concentrations ranging from 2·5–12·5 moles per mole of mercuric chloride the virus became reactivated, and titres of $1{\cdot}3 \times 10^2$–$9{\cdot}3 \times 10^2$ units per ml. were attained. Reactivation was also obtained with sodium thioglycollate. It was not possible to restore the activity of vaccinia virus inactivated with thiomersalate or phenylmercuric borate. The ease with which reactivation could be brought about suggested that the sulphydryl groups attacked by mercury are placed superficially, and may be involved in the attachment of the virus particle to the cell. *D. J. Bauer*

Roizman, B., Hoggan, M. D. & Cornfield, J. **Linear and Parabolic Estimates of the Titers of Herpes Simplex from Pock Counts on the Chorioallantoic Membrane of Embryonated Eggs.** *Virology.* New York. 1960, July, v. 11, No. 3, 572–89, 2 figs. [10 refs.]

" Analysis of 33 randomly selected titrations of herpes simplex on chorioallantoic membranes of embryonated hens' eggs revealed that the variance of pock counts among replicate eggs was considerably higher than expected and that the mean pock counts at high concentrations of virus were less than predicted from counts obtained following infection at low concentration of

virus. The curve relating mean pock count to virus concentration levelled off in 26 titrations. The deviation was significant in 4 of the titrations. The upper limit of the linear portion of the dose response curve as defined in the text varied from 11 to 1100 mean pocks per membrane. Methods for estimating virus titres based on linear and parabolic approximations of the pock count-dose relationship were described and compared. The parabolic approximation was recommended for studies in which a more precise estimate of virus titre was desired."

BURKE, D. C. & ISAACS, A. **Interferon: Relation to Heterologous Interference and Lack of Antigenicity.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 215–19. [18 refs.]

Some experiments are reported in support of the hypothesis that interferon is the mediator of "heterologous virus interference", induced by exposing cells to inactivated virus before another active virus is added. It is shown first that the smallest amount of inactive virus which induces a marked degree of interference also leads to the production of interferon [but in cultures in which there was a lesser degree of interference no interferon was detected]. It is shown secondly that Sendai, MEL and fowl plague virus show decreasing sensitivity to both interference by ultraviolet inactivated virus and to interferon. There are other experiments to show that interferon prevents the formation of "soluble" influenza virus antigen. [The test for "soluble" antigen would have been more specific if ultracentrifugation or a specific animal serum had been used.] Repeated attempts have failed to demonstrate that purified chick interferon is antigenic for rabbits. *D. A. J. Tyrrell*

RÁTOVÁ, V., KOCISKOVÁ, D., SZÁNTÓ, J., LAUCIKOVÁ, O. & HÁNA, L. **Certain Properties of the Virus-Neutralizing Factor of Normal Animal Sera.** *Problems of Virology.* London. 1959, v. 4, No. 6, 86–92, 1 fig. [15 refs.] [Translated from Russian.]

It has been suggested that the β inhibitors of normal sera, which neutralize various myxoviruses, may be properdin or some part of the properdin system [this *Bulletin*, 1957, v. 32, 517].

The authors have attempted to clarify the question of the nature of the β inhibitor by titrating various normal animal and human sera for their content of properdin, complement, C'3, and virus neutralizing and haemagglutination-inhibiting activity. Heated sera and sera treated with zymosan were also titrated. The results are in general agreement with previously published work. It was shown that guineapig serum contained a heat-stable virus-neutralizing inhibitor for A2 influenza but that otherwise the normal inhibitors were heat-labile and removed by zymosan treatment, like properdin. They were precipitated by $(NH_4)_2SO_4$ with the beta or gamma globulins. The sera used inhibited the enzymic activity of influenza viruses and in some cases this inhibitory activity was reduced by heating and occasionally by removal of properdin.

[There seem to be some errors in the $>$ and $<$ signs in Table 2]. *D. A. J. Tyrrell*

COHEN, A. & BIDDLE, F. **The Effect of Passage in Different Hosts on the Inhibitor Sensitivity of an Asian Influenza Virus Strain.** *Virology.* New York. 1960, June, v. 11, No. 2, 458–73, 2 figs. [26 refs.]

γ inhibitor, present in normal horse serum, inhibits both haemagglutination and infectivity of Asian influenza virus strains [this *Bulletin*, 1959, v. 34, 688]. The egg-adapted A/Singapore variant was adapted to mouse lung in 2 lines, A and B, the mice being inoculated intranasally. Mouse pathogenicity was expressed as a percentage of lung surface consolidated and not until the 22nd and 47th passages were lung lesion scores over 80% in lines A and B, respectively. During this adaptation, egg neutralization tests on arbitrarily picked 25th and 26th passage viruses of line A demonstrated a loss of sensitivity to γ inhibitor. Mouse lung suspensions contained insufficient virus for haemagglutination so that a further egg passage was necessary. The product, $E_3M_{26}E_1$ "A", was insensitive to horse serum in the neutralization test, but highly sensitive in the HI test. With the limit-dilution technique using eggs, $E_3M_{26}E_1$ "A" was shown to be a mixture of sensitive and resistant particles, which accounted for its behaviour. The passage of $E_3M_{26}E_1$ "A" at low dilution (10^{-2}) in eggs and mice led to virus populations highly sensitive and resistant respectively. Further evidence that the resistant particles survived better in mouse lung was that continued passage of mouse line A resulted in a virus population almost completely sensitive to horse serum in both neutralization and HI tests. These data indicated that changes of inhibitor sensitivity resulted from changes in the proportion of sensitive and resistant particles. Line B behaved differently, the 34th and 51st passage viruses being highly sensitive in both neutralization and HI tests.

The problem remained whether resistant particles in undetectable numbers were present in the egg-adapted virus before mouse passage, or arose by mutation. The former possibility was tested by serial passage of the egg-adapted virus in the presence of increasing concentrations of horse serum. A completely resistant virus population was not obtained until after the 4th passage, and moreover, there was a gradual decrease in sensitivity to inhibitors in sera from different animal species. The authors suggest that particles of variable inhibitor sensitivity were produced by mutation.

No correlation was demonstrated between inhibitor sensitivity and enzymatic activity [*ibid.*, 1957, v. 32, 1201], as measured by the elution rate from fowl and human red cells, or sensitivity to specific antibody in the HI test. *D. Taylor-Robinson*

COHEN, A. **Protection of Mice against Asian Influenza-Virus Infection by a Normal Horse-Serum Inhibitor.** *Lancet.* 1960, Oct. 8, 791–4, 1 fig. [23 refs.]

Certain influenza A2 virus strains were inactivated by an inhibitor (γ inhibitor), present in normal horse serum,

which is not apparently antibody and is inactivated by treatment with periodate but not with the receptor destroying enzyme. Mice were inoculated intranasally with $10^{2.4}$ LD50 of an inhibitor-sensitive strain of influenza A2 virus. Intravenous administration of 0·25 ml. of serum had no effect but mice receiving 0·05 ml. of serum intranasally between 48 hours before and 3–6 hours after infection were protected from the lethal effect of the virus, though mice receiving serum after the virus developed quite extensive lung lesions. The author considers that these experiments indicate that intranasal administration of normal horse serum or a refined fraction from it might be of value in preventing influenza in man. [It should be pointed out that not all influenza A2 virus strains are susceptible to this inhibitor, and pre-1957 strains are all insensitive. Moreover, dangerous allergic reactions have followed the intranasal inoculation of horse serum in man.] *D. A. J. Tyrrell*

Reznikova, O. I. & Avrorova, R. I. **Characteristics of Strains of Influenza Virus isolated in Rostov-upon-Don in 1957.** *Problems of Virology.* London. 1959, v. 4, No. 5, 82–7, 1 fig. [Translated from Russian.]

During an influenza epidemic, most marked in October 1957, virus was isolated on 21 occasions from 87 nasopharyngeal washings inoculated into the amniotic cavity of 10- to 11-day-old chick embryos. 12 of these strains were studied in more detail. Haemagglutination of chick cells produced by 10 of the 12 strains was not inhibited by immune sera (rat) to the reference strains A, A-prime, B (Kri), C and D (Sendai) and only 4 strains were inhibited by A2 Singapore antiserum. However, since immune sera to the newly isolated strains R7, R10, R30, and R46 inhibited to various degree A2 Iksha and A2 96 Leningrad strains and also 11 of the newly isolated strains the latter were classified as belonging to A2 influenza virus type. *D. Taylor-Robinson*

Paucker, K. **Apparent Antigenic Change in a Laboratory Line of Influenza A Virus during Continued Propagation in Chick Embryos.** *J. Immunology.* 1960, Aug., v. 85, No. 2, 148–62, 6 figs. [23 refs.]

A strain of PR8 virus was sent to Copenhagen in 1941 and has since been passed there on numerous occasions. It was recently found to be antigenically different from lines passed in other laboratories and from virus set aside from earlier passes made in the same laboratory. The antigenic composition and behaviour of the virus has been exhaustively studied by haemagglutination inhibition methods, with chicken sera before and after absorption with viruses. It is concluded that the antigenic change occurred because a mutant arose at about the 130th passage in eggs, which subsequently replaced the original serotype. It is thought that substitution of another strain, or contamination and recombination with another virus have been excluded. [Those interested should read this very detailed paper in the original.]
D. A. J. Tyrrell

Yakhno, M. A., Zakstel'Skaia, L. I. & Zhdanov, V. M. **The Receptor Activity of Influenza and Influenza-Like Viruses.** *Problems of Virology.* London. 1959, v. 4, No. 6, 10–17, 1 fig. [Translated from Russian.]

The authors have extended the work of Burnet on the receptor gradient to include myxoviruses undiscovered at the time of his experiments and not otherwise exhaustively tested in this respect. The "new" viruses tested were influenza A2 Sendai (influenza D), influenza C, horse influenza, HA1 and HA2 (of Chanock). In preliminary experiments it was found that some viruses were haemolytic, namely Sendai and avid influenza A2; non-avid influenza A2 was not haemolytic. Influenza C fell beyond mumps virus at the end of the "Burnet" gradient; Sendai, horse influenza and non-avid influenza A2 fell between Newcastle disease virus and influenza A in that order. Avid influenza A2 fell beyond the other end of the scale since cells treated by this virus were not agglutinated by any other virus used.

The HA1 and HA2 viruses seemed to fall outside this pattern altogether as cells treated by them were fully agglutinable by all heterologous viruses, and cells treated by heterologous viruses were agglutinable by HA1 or HA2. [It has been shown, of course, that receptors for HA1 and HA2 are destroyed by cholera filtrate.] Adsorption elution curves were constructed for some of the viruses and it was found that avid influenza A2 virus was rapidly absorbed and slowly eluted, like its neighbours in the receptor gradient, whereas non-avid A2 virus was poorly absorbed and rapidly eluted like mumps and NDV.

[In fig. 1, the ordinates should read "haemagglutination" and not "inhibition". This paper is interesting and worth reading in full. It is of interest that although the Sendai and HA2 viruses are related serologically, and avid and non-avid influenza A2 are antigenically identical, yet in these tests the members of the pairs behave very differently from each other.]
D. A. J. Tyrrell

Smith, D. H. & Morgan, H. R. **A Cytopathogenic Effect of Influenza Virus (PR-8 Strain) for Mouse Fibroblastic (L) Cells *in vitro*.** *J. Immunology.* 1960, Aug., v. 85, No. 2, 180–89, 7 figs. [21 refs.]

When large doses of the PR8 strain of influenza A virus are inoculated to L cells growing on glass, the cells degenerate. This phenomenon has been studied in some detail. The degeneration is prevented by exposing the cells to RDE or heat-inactivated virus, before toxic virus is inoculated; degeneration is also prevented by heating the virus, treating it with homologous antiserum, or irradiating it with UV light to an extent similar to that required to destroy infectivity for eggs. It was shown that the added virus was absorbed to cells, entered them, and then underwent a sort of virus growth in which haemagglutinin was produced but little infectious virus.
D. A. J. Tyrrell

HOWE, C., LEE, Lucille T. & ROSE, H. M. **Influenza Virus Sialidase.** [Correspondence.] *Nature.* 1960, Oct. 15, v. 188, 251–2, 1 fig.

GAIDAMAKA, M. G., DROMASHKO, A. S. & FIADINA, D. D. **A Glycerolated Diagnostic Influenza Antigen.** *Problems of Virology.* London. 1959, v. 4, No. 6, 30–36. [Translated from Russian.]

Allantoic fluid containing influenza virus, after centrifugation at 2,000 r.p.m. for 20 minutes, was placed in a Cellophane sac and dialysed against 4–6 times its volume of glycerol at 5°C. for 18 hours. A-prime, A2, B and D glycerolated influenza antigens were produced in this way, the volume of fluid decreasing 5- to 9-fold and the haemagglutinin titre increasing 4- to 8-fold. The preparations were stable after storage at 5°C. for 13 months as there was no fall in haemagglutinin titre but there was a 4- to 8-fold fall in titre of A-prime and one A2 strain after 10 months at 22–28°C. The glycerolated antigens produced approximately the same results in complement-fixation tests with paired influenza sera as soluble S antigens. *D. Taylor-Robinson*

THIBON, M. Action du benzo-dodécinium sur la multiplication du virus grippal. [**Action of Benzo-Dodecinium on Influenza Virus**] *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 414–20, 1 fig.

Dodecyl-dimethyl-benzyl-ammonium (BD) at a final concentration of 0·0075% was shown to inactivate the infectivity of PR8 influenza virus. 0·1 ml. of a solution of 0·025% failed to prevent virus multiplication in the allantoic cavity of the developing egg. Mice were infected by aerosol with the same virus and exposed once or twice to an aerosol of 0·015% or 0·025% BD at various times after inoculation. 17 dosage schemes were tried on groups of 10 mice each and it appears that with 11 of these 20% to 50% of the treated mice survived longer than the control mice; ultimately all treated mice except one died. With one dosage scheme (treatment 2 and 4 hours after virus infection) 3 of 10 mice recovered. *D. A. J. Tyrrell*

MASON, E. J. & KAUFMAN, N. **The Toxic Properties of Massive Inoculums of Newcastle Disease Virus and Influenza Virus (PR8) for Cell Strains derived from Normal and Neoplastic Tissue.** *Amer. J. Path.* 1960, Aug., v. 37, No. 2, 231–43, 5 figs. on pl. [18 refs.]

Newcastle disease virus and PR8 influenza virus, contained in allantoic fluid, produced "toxic" changes when inoculated at concentrations of $10^{6.5}$ egg-infectious doses into murine L, $LLCM_1$ and Sarcoma 180 and human U_{1_0} and KB cultures containing $10^{5.5}$ cells per tube. This represented a 1/1,000 dilution of the allantoic fluids. Dilutions exceeding this were frequently without effect; a 1/5 dilution, however, caused complete destruction in about 24 hours. This was due to infective virus since normal allantoic fluid or infected fluid that had been heated to 56°C. for 30 minutes caused no cell destruction and the effect was neutralized by specific immune sera. It was assumed that intracellular virus multiplication did not account for the cell destruction because low concentrations of either virus did not destroy cells after 5 days and the cytotoxic effect was not serially transmissible. [Others, *e.g.* HENLE and HENLE (this *Bulletin,* 1955, v. 30, 645) have shown that under these conditions influenza virus undergoes an abortive multiplication cycle, in which haemagglutinin and soluble antigen are formed but not infectious virus.] *D. Taylor-Robinson*

GARDNER, P. S. **A Serological Relationship between Mumps and Sendai Viruses.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 283–9.

66 paired sera from patients with mumps were examined for complement-fixing (CF) antibodies with mumps and Sendai virus particle (V) antigens and most sera with mumps soluble antigen. 31 cases showed a 4-fold or more increase in antibody with mumps V antigen but no increase when tested with Sendai antigen and 35 cases showed a 4-fold or greater antibody rise with both V antigens. The occurrence of both antibodies was further shown in an examination of 978 antenatal sera. 4% of these were positive to mumps V antigen only and 17% to Sendai only; 9% were positive to both antigens. Of 362 blood transfusion sera, 4% were positive to mumps V antigen and 10% to Sendai only and 5% were positive to both. Chessboard titration of mumps paired sera showed at least a 4-fold increase in antibodies to both Sendai and mumps V antigen and both antigens gave their expected optima. The author considered that this showed the independent action of the 2 antibodies.

The possible explanation of the formation of the 2 distinct antibodies during mumps infection were considered. Of 13 patients whose sera showed a 4-fold or greater rise in mumps CF antibody, 6 had a Sendai CF antibody titre of 1 in 8 or more in the acute phase serum (therefore recently infected) but showed no rise in the convalescent serum. This discounted the possibility of mumps virus calling forth an anamnestic response in people recently infected with Sendai virus. The author discusses and rejects the possibility of there being 2 antigenic forms of mumps virus, one containing a Sendai virus component and the other not and concludes that mumps and Sendai viruses share an indistinguishable common antigenic component. *D. Taylor-Robinson*

LÉPINE, P. & BONISSOL, C., with the technical collaboration of P. KONA. Respiration et glycolyse de cellules KB infectées par *Myxovirus parainfluenzae* type III. [**Respiration and Glycolysis of KB Cells infected with *Myxovirus parainfluenzae* Type III**] *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 440–43, 1 fig.

The English summary appended to the paper is as follows:

"O_2 uptake of KBEa cells infected with Ea 102 virus and O_2 uptake of normal KB cells are identical.

"Aerobic glycolysis of infected cells is markedly higher than that of normal cells."

ENJALBERT, Lise, DIDIER, Jacqueline, LARENG, Marie B. & LAPCHINE, Lydia. Les adénovirus. Étude de 17 souches isolées à Toulouse. [**Adenoviruses. Study of 17 Adenovirus Strains isolated at Toulouse**] *Ann. Inst. Pasteur.* 1960, Oct., v. 99, No. 4, 608–17, 4 figs. on pl. [24 refs.]

PHILIPSON, L. & CHOPPIN, P. W. **On the Role of Virus Sulfhydryl Groups in the Attachment of Enteroviruses to Erythrocytes.** *J. Exper. Med.* 1960, Sept. 1, v. 112, No. 3, 455–78, 5 figs. [37 refs.]

"A number of sulfhydryl reagents prevented agglutination of erythrocytes by enteroviruses. Detailed studies with *p*-chloromercuribenzoate (PCMB) showed that inactivation of viral hemagglutinating activity was due to the failure of PCMB-treated virus to adsorb to erythrocytes. The various sulfhydryl reagents appeared to react with sulfhydryl groups on the virus particle.

"Inactivation of the hemagglutinating activity of enteroviruses by mercaptide-forming agents was reversed by thiol compounds. The results suggest that sulfhydryl groups are involved in the attachment of enteroviruses to erythrocytes. In addition to the prevention of adsorption to erythrocytes, the infectivity of several enteroviruses was decreased by sulfhydryl reagents."

DARNELL, J. E., Jr. & SAWYER, T. K. **The Basis for Variation in Susceptibility to Poliovirus in HeLa Cells.** *Virology.* New York. 1960, Aug., v. 11, No. 4, 665–75, 1 fig. [23 refs.]

HeLa cells of clone I–3 produce approximately 6–10 times as many poliovirus plaques as those of strain S3–1. It was found that poliovirus adsorbed to both cell clones in suspended culture at about the same rate. Penetration of virus into the cells beyond the reach of antiserum was equally rapid in both cell clones. Also with both cells about 95% of the virus adsorbed could not be recovered from the cells by freezing and thawing. However, in monolayer cultures it was found that both clone I–3 and a sub clone of S3–1 called S3–1c obtained by selecting cells failing to be destroyed by poliovirus, gave similar numbers of plaques when infected with RNA derived from poliovirus. It is therefore surmised that in the relatively insensitive cells infectious nucleic acid is not so efficiently released from the virus that penetrates the cells.

A. J. Beale

SELZER, Golda. **The Use of New Antigens in the Complement-Fixation Test for Acute Poliomyelitis.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 321–30.

The author has previously described the adaptation of types 1 and 2 poliovirus to suckling mouse brains [SELZER *et al.*, this *Bulletin*, 1952, v. 27, 897 and SELZER and BUTCHART, *Ibid*, 1960, v. 35, 314]. One of the objects was to prepare good antigens for complement-fixation tests for the diagnosis of poliovirus infection. Antigens from brain were treated with acetone and ether, and saline extracts were used as antigen after clarification. With these antigens homotypic antibodies were found in all of 53 patients from whom type 1 and type 2 poliovirus or both were isolated. The acute phase sera very often showed a positive reaction. Only 15 of the 53 patients failed to show antibodies in the first sample. 31 of 45 sera tested in the 3rd or 4th week showed a rise in titre in convalescence. 37 of the 52 cases (1 case had simultaneous 1 and 2 poliovirus infection) showed a specific monotypic antibody response. Heterotypic antibodies were generally of low titre and stationary. In sera from 26 control subjects, 7 showed antibodies. 1 was considered non-specific and 1 patient was probably infected with poliovirus since he had a high titre of poliovirus antibodies. The results obtained in six patients from whom no virus was isolated are given. 4 probably had type 1 infection and 1 type 2 whereas 1 patient with bulbar "poliomyelitis" had no poliovirus neutralizing or CF antibodies and presumably was not infected with this virus.

In general heating did not broaden the specificity of the antigens although antibody titres were generally lower. The author concludes that these new CF antigens are valuable aids to the laboratory diagnosis of poliomyelitis. They are considered to be superior to those derived from tissue cultures since both the antigen titres and serum titres are higher with these antigens.

A. J. Beale

AGNESE, G. & CROVARI, P. Sulla titolazione degli anticorpi neutralizzanti antipoliomelitici in rapporto alla quantità di virus presente nelle miscele. [**On Titration of Poliomyelitis Neutralizing Antibodies in relation to Quantity of Virus present in the Mixtures**] *Ann. Sclavo.* Siena. 1960, Mar.–Apr., v. 2, No. 2, 151–68, 1 fig. English summary.

The investigation has been made of the optimum conditions for carrying out neutralization tests with type 1 poliomyelitis virus in cultures of KB cells. Serial 2-fold dilutions of a type 1 antiserum were incubated with a constant dose of type 1 virus for 4 hours at 37°C., and the residual unneutralized virus was then titrated by adding KB cells. The titration was carried out in 7 replicates with doses of virus varying over a 64-fold range. The neutralization titres observed for the antiserum had a linear regression upon the logarithm of the dose of virus with a negative slope, the value of the regression coefficient being –0·594. In similar experiments with types 2 and 3 virus regression coefficients of –0·458 and –0·433 were obtained. The authors suggest that the titre observed experimentally should be adjusted to the value corresponding to a standard dose of virus by using the regression line, and a formula for carrying out this correction is given. A dose of 10 TCD50 is probably the lowest which will give satisfactory results in practical conditions.

D. J. Bauer

JEZIERSKI, A. **Destruction of Poliovirus in the Digestive Tract of Chimpanzees by means of Specific High-Titre Gamma-Globulin.** *Ann. Soc. Belge de Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 169–71. Discussion [in French] 172–81.

Gamma globulin prepared from poliovirus immune serum of high titre from the ass was found to limit intestinal infection with polioviruses in the chimpanzee. After a daily dose of 35–50 ml. of gamma globulin by mouth for 2–18 days virus excretion usually ceased in a few days but was occasionally seen for 18 days. In the absence of treatment virus excretion occurred for at least 21 days. In 2 human subjects given 2 daily 50 ml. doses of gamma globulin specific antibodies were found in faecal extracts 24 hours later. This work is vigorously criticized in discussion by L. MORTELMANS and by P. BRUTSAERT for lack of details which were later supplied. It is thought, by them, unlikely that antibodies would survive denaturation due to digestive enzymes. Also, since circulating antibodies evinced by Salk vaccine do not affect poliovirus excretion, it is thought unlikely that orally administered antibody would be any better. Insufficient attention has been given to the possibility that viral interference may have played some part in clearing poliovirus from these animals. In the main experiment reported a mixture of all 3 types of poliovirus was used and this complicates the interpretation. *A. J. Beale*

SOLOVYOV, V. D. & GULEVICH, N. E. **Studies on Antiviral Immunity using Tissue Culture Methods. II. Obtaining Cells resistant to Poliomyelitis Virus.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 220–26, 8 figs. (6 on 3 pls.)

From one tube of a culture of a human leukaemic cell line J-96 (OSGOOD and BROOKE, *Blood*, 1955, v. 10, 1010) infected with 10^5 TCD50 of Brunden type 1 poliovirus a strain of cells, LBV, resistant to Brunden virus was isolated 45 days after inoculation and after 2 medium changes. First 1 and then 2 colonies grew out in the culture. These cells initiated the LBV line. It proved equally as sensitive as the parental J-96 cells [here sometimes called L cells, which may cause confusion with Earle's mouse fibroblast cells of the same name] to vaccinia, adenovirus type 7, Coxsackie B3 and ECHO 9 viruses, but the sensitivity to Brunden type 1 poliovirus of the LBV cells was much less. A similar, though less marked, effect was noted against types 2 and 3 poliovirus. Extensive efforts to identify a hypothetical latent poliovirus infection of the cells failed. During continued passage of LBV cells they partially lost their relative resistance to poliovirus infection. The authors explain their observations as specific cellular immunity not related on the one hand to viral interference nor on the other to the selection of a resistant cell population from the J-96 cells. [See this *Bulletin*, 1960, v. 35, 1066.]

A. J. Beale

NOSIK, N. N. **The Influence of Cortisone on Vaccination Immunity towards Poliomyelitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 12, 98–102, 2 figs. [19 refs.] [Translated from Russian.]

"(1) Treatment with cortisone in the vaccination period caused a decrease in the immunity of mice due to vaccination.

"(2) The level of immunity approached zero when cortisone was injected 6 days after vaccination.

"(3) Divided doses of cortisone given during the vaccination period suppressed the formation of neutralizing antibodies, whereas equivalent single doses given in the same period did not affect the antibody formation.

"(4) Cortisone given 6 days after vaccination reduced the titres of antibodies in all groups."

DUNCAN, I. B. R. **Aseptic Meningitis associated with a Previously Unrecognised Virus.** *Lancet.* 1960, Aug. 27, 470–71.

In 1959 during an outbreak of aseptic meningitis in Central Scotland a new virus was isolated from 37% of the cases. This virus is called Frater virus. It has the characteristics of a new member of the ECHO group of enteroviruses. It is not neutralized by antisera to poliovirus type 1, 2 or 3, Coxsackie A7 or 9, B 1–6, ECHO 1–27. ECHO 28 (MOGABGAB and PELON'S 2060, *Ann. N.Y. Acad. Sci.*, 1957, v. 67, 403) produces a different sort of cytopathic effect. The infected tissue culture fluid was a satisfactory CF antigen with specific antisera, but did not fix complement with adenovirus or herpes simplex antisera. Pooled human gamma globulin neutralized Frater virus to a titre of 1 in 32. The evidence that the virus caused aseptic meningitis is as follows: it was isolated from 37% of the cases and 6% of the controls; serological evidence confirmed 41 out of 48 cases from whom virus was isolated and added 8 more cases (evidence was either a rise in titre or a convalescent level over 1 in 64; a titre of 1 in 16 was never exceeded in a sample of 117 blood donor sera taken six months before the outbreak occurred). The virus was isolated from a child, 1 year old, with paralysis. This child had no virological evidence of poliovirus infection. The titre of Frater virus is higher in human thyroid than in amnion and in amnion than in monkey kidney cells by 10–100 fold in each case. Similarly, when 75 known Frater positive stools were tested in the 3 sorts of cells, 65 were isolated in thyroid, 58 in amnion and 26 in monkey kidney cells. Frater virus is now being examined by the Chairman of the National Foundation Committee on Enteroviruses. *A. J. Beale*

SVET-MOLDAVSKY, G. J., SVET-MOLDAVSKAYA, I. A. & KISELEVA, I. S. **Preparation of Allergen-Free Vaccines against Transmissible Encephalitides and Rabies from the Brain of Suckling Mice and Rats.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 320–22. [11 refs.]

Freund's adjuvant containing tubercle bacilli was mixed with an equal volume of 50% brain and 5 simultaneous injections of 0·2 ml. were given subcutaneously to guinea-pigs. No allergic encephalomyelitis was caused by brain from rats aged 4–16 days while 7 of 9 inoculated with brain of rats aged 8 weeks succumbed. Similarly brains of mice aged 5 and 10 days caused no encephalomyelitis

while 5 of 12 inoculated with brain from 6 week-old mice succumbed. If suckling rats and mice are used in the preparation of brain tissue vaccines the probability of paralytic accident should be much less than if adult rat- and mouse-brains were used. *C. E. Gordon Smith*

SPITSYNA, L. N. **Immunological Characteristics of a Natural Focus of Tick-Borne Encephalitis.** *Problems of Virology.* London. 1959, v. 4, No. 6, 36–40. [23 refs.] [Translated from Russian.]

"(1) A natural focus of tick-borne encephalitis in the village of Golyi Mys in the Perm Oblast' proved to be potentially highly active from an immunological point of view.

"(2) The fact that a considerable percentage of serological reactions were positive in persons who had not been suffering from tick-borne encephalitis and in domestic animals (cows and goats) shows that infected ticks have been wide spread in the focus in question over a number of seasons.

"(3) Comparison of the data characterizing the immunological state of the population in the focus in question with the number of diagnosed cases of tick-borne encephalitis (sporadic cases) warrants the conclusion that tick-borne encephalitis occurs in the Goyli Mys focus most frequently in the form of subclinical infections."

GAIDAMOVICH, S. I. & OBUKHOVA, V. P. **The Use of Tissue Cultures for the Indication of Sublethal Doses of Tick-Borne Encephalitis Virus.** *Problems of Virology.* London. 1959, v. 4, No. 6, 41–7, 2 figs. [Translated from Russian.]

"The infection of chick embryo fibroblast cultures is a sensitive method for the detection of small doses of tick-borne encephalitis virus."

ANAN'EV, V. A. **The Effect of Hydrogen Peroxide upon Tick-Borne Encephalitis Virus.** *Problems of Virology.* London. 1959, v. 4, No. 6, 47–50. [Translated from Russian.]

"(1) Hydrogen peroxide in a concentration of 2–3 per cent has a virucidal activity upon tick-borne encephalitis virus.

"(2) The inactivation of the virus by hydrogen peroxide can be considerably increased by the presence of peroxidase (horse-radish extract).

"(3) Freshly prepared horse-radish extract has a virucidal effect upon tick-borne encephalitis virus."

KARPOVICH, L. G. & LEVKOVICH, E. N. **The Differentiation of Tick-Borne Encephalitis and Louping-Ill Viruses in Tissue Culture.** *Problems of Virology.* London. 1959, v. 4, No. 5, 60–65, 3 figs. [Translated from Russian.]

"(1) Human tick-borne encephalitis and louping-ill virus undergo active multiplication in HeLa cultures.

"(2) Louping-ill virus unlike tick-borne encephalitis virus exerts a marked cytopathogenic effect on HeLa cells; the specific character of this effect can be confirmed by the fact that the homologous immune serum, as well as immune serum for tick-borne encephalitis virus inhibits the cytopathogenic effect.

"(3) The different susceptibilities of HeLa cells to tick-borne encephalitis and louping-ill viruses can be used for the differentiation of these two viruses."

KORYCH, B. Možnosti kultivace viru klíštové encefalitidy na tkánových kulturách stabilní linie epitelu vepřové ledviny (PK). **[The Possibility of Cultivating Tick-Borne Encephalitis in Virus Tissue Cultures of a Stable Line of Pig Kidney (PK) Epithelium]** *Československ. Epidemiol., Mikrobiol. Imunol.* Prague. 1960, v. 9, No. 4, 282–5. English summary (8 lines).

The Hypr and HA mouse-adapted strains of tick-borne encephalitis virus have been successfully grown in PK cells, a continuous cell line derived from the cortex of the pig kidney. The Hypr strain caused massive cell destruction at the first passage, and attained a titre of $10^{4.83}$ in PK cell cultures and 10^5 in mice. The HA strain behaved similarly, but grew more slowly and had a somewhat lower titre. *D. J. Bauer.*

MÁLKOVÁ, D. **The Role of the Lymphatic System in Experimental Infection with Tick-Borne Encephalitis. I. The Tick-Borne Encephalitis Virus in the Lymph and Blood of Experimentally Infected Sheep.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 233–40, 4 figs. (1 on pl.)

The Hypr strain of tick-borne encephalitis virus after 40–43 mouse passages was inoculated into sheep with a cannula in the thoracic duct so that the lymph could be sampled and, where required, prevented from entering the bloodstream. A large dose of virus was given into a peripheral lymph vessel in the left hind limb of a sheep in which the lymph was not allowed to enter the bloodstream: lymph from the thoracic duct and blood from the metatarsal vein were examined for virus. It was found only in the lymph 6–72 hours after infection, maximal at 48 hours. Virus was found in the regional lymph nodes but not in the viscera up to 7 days after infection. Virus thus seems to reach the blood from the lymph only through the thoracic duct. In similar experiments where the lymph was allowed to flow from the thoracic duct into the bloodstream, virus appeared first (4 hours) in the lymph then in the blood (8 hours). The titre in the lymph was consistently higher than in the blood. When the blood was sampled from a contralateral vein it was detected at 16 hours. After 72 hours titres fell both in blood and lymph and could not be detected from 120 hours onward.

After subcutaneous inoculation of a large dose of virus, it appeared first in the lymph (1 hour) then in the blood (4–8 hours). The titres in lymph were higher than in blood and both declined after 96 hours. In sheep

which died or were killed the organs were titrated for virus—it was found only in the lymph nodes and spleen. Sheep were re-infected 7 and 12 days after first infection: no virus was detected in lymph or blood from 30 minutes to 48 hours after re-infection.

Virus thus appears to be carried to the blood through the lymphatics and in animals such as sheep which are not highly susceptible to peripheral infection virus seems to be confined mainly to lymphatic organs.

C. E. Gordon Smith

MÁLKOVÁ, D. **The Role of the Lymphatic System in Experimental Infection with Tick-Borne Encephalitis. II. Neutralizing Antibodies in the Lymph and Blood Plasma of Experimentally Infected Sheep.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 283–9, 4 figs.

Neutralizing antibodies were studied in sheep with cannulated thoracic ducts no longer connected to the blood circulation [see above]. After inoculation of a large dose of the H strain of tick-borne encephalitis virus by various routes, neutralizing antibody was detected first in the lymph (by 72 hours after infection) where it reached a maximum after 96–144 hours; the appearance of detectable antibody closely followed the fall in titre of virus in the lymph. Neutralizing antibody became detectable rather later in the blood (96–120 hours) and reached its maximum later (144 hours or later) at about the same titre as the lymph. Again the appearance of antibody followed closely the fall in viraemia. When a second dose of virus was administered after an interval there was an increase of antibody in both blood and lymph sometimes more marked in the former. *C. E. Gordon Smith*

MÁLKOVÁ, D. **Participation of the Lymphatic and Blood Circulations in the Dissemination of Tick-Borne Encephalitis Virus to the Organs of Experimentally Infected Mice.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 290–95.

Strain H of tick-borne encephalitis virus (41–45th mouse passage) was inoculated by the intraplantar route in mice; the mice were bled and various organs were dissected out at intervals after inoculation: these were titrated by intracerebral mouse-inoculation. 6 hours after inoculation virus was not detected. After 12 hours virus was found only in the blood. After 24 hours the viraemia increased and virus was detected in the spleen and liver. After 48 hours virus was also found in lung, myocardium and brain in low titre and in high titre also in the inguinal lymph nodes. After 72–96 hours virus was present in most organs. After 192 hours virus had almost disappeared from the blood and for the first time reached a high titre in the brain, persisting in most of the organs. The disappearance of viraemia coincided with the appearance of neutralizing antibody in the blood. The process of spread was slightly more rapid in younger than in older mice. At a late stage of the infection the virus titre in the organs depended on the amount of circulating antibody. *C. E. Gordon Smith*

BENDA, R. & DANES, L. **Study of the Possibility of preparing a Vaccine against Tick-Borne Encephalitis, using Tissue Culture Methods. III. Experimental Principles for Safety Tests of Virus Inactivation in Formolized Liquids.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 296–307. [23 refs.]

Tests were made on a formalinized vaccine prepared from the fluid of chick embryo fibroblast cultures infected with the B3 strain of tick-borne encephalitis virus after 10–15 mouse passages. Comparative titrations of virus suspensions were made in weaned and suckling (4–6 day) mice with and without cortisone treatment followed by blind passage on the 5th, 8th and 12th days. Cortisone-treated weaned mice seemed to be slightly more sensitive than untreated weaned mice. Cultures of SCH (monkey heart) cells with inoculation of the culture fluid into mice at intervals appeared to be as sensitive. Fourteen formalin-treated fluids were tested 6–10 days after the start of treatment for residual virus: 4–6-day mice were more sensitive than weaned mice when inoculated intracerebrally. Cortisone-treated mice and SCH cells both with passage into mice were the most sensitive methods of detecting residual live virus. It was necessary to dialyse fluids to remove formalin before inoculating them into tissue-cultures. 8 formalin-treated fluids were tested after 19–40 days' treatment: the batches were of 500–1,000 ml. and about 50 ml. were tested in untreated and cortisone-treated mice, 18–30 ml. in cell cultures. No live virus was detected in any of these 8 fluids. *C. E. Gordon Smith*

VILCEK, J. **Interference between Tick-Borne Encephalitis and Western Equine Encephalomyelitis Viruses in Chick Embryo Tissue Cultures.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 308–10.

Tube cultures of chick-embryo fibroblasts were infected with dilutions of the Hypr strain of tick-borne encephalitis virus. 24, 48 and 72 hours later 320 TCD50 of western equine encephalitis virus were added. Tick-borne encephalitis virus multiplies in chick-embryo fibroblasts but does not cause cytopathic effects. Western equine virus causes complete destruction of the cells. When western equine virus was added 24 hours after tick-borne virus there was no inhibition of cytopathic effect, at 48 hours there was partial inhibition, and at 72 hours there was complete inhibition of cytopathic effect in tubes infected with tick-borne virus. This system was used to titrate mouse-adapted Hypr, HeLa-adapted Hypr, and the KEm, strains of tick-borne encephalitis virus, louping ill and Kyasanur Forest disease virus. The titres were compared with parallel titrations in mice by the intracerebral and intraperitoneal routes. Titres obtained by the western equine interference method in chick-embryo fibroblasts were very close to those obtained by intracerebral titration in mice and as high or higher than those by intraperitoneal inoculation. Neutralization tests with specific gamma globulin could also be performed thus in chick-embryo fibroblasts. Preliminary experiments suggested that high doses of Hypr virus in chick-embryo

fibroblasts caused the production of "interferon"-like material. *C. E. Gordon Smith*

COLLIER, W. A. & DE WIT, M. Die Züchtung des Gelbfiebervirus 17D im Ascites des Krebs-2-Carcinoms. **[Cultivation of the 17D Strain of Yellow Fever Virus in the Ascites Form of the Krebs 2 Carcinoma]** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 2, 209–23, 11 figs. [47 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 48.]

RIAZANTSEVA, N. Y., SMIRNOVA, Y. V. & KOZLOVSKAIA, L. A. **Influence of the State of Maternal Immunity to Measles on the Immunity of the Child. Experiments on Monkeys and Small Laboratory Animals.** *Problems of Virology.* London. 1959, v. 4, No. 1, 59–63. [Translated from Russian.]

In experiments on monkeys and other animals, the authors have investigated the transfer of maternal immunity to measles to the offspring. 3 of 4 offspring born to monkeys which were immune to measles before the beginning of pregnancy developed the disease when challenged with live measles virus in the 3rd–4th month of life, whereas the remaining young animal was immune when challenged during the 1st month, but susceptible after 18–22 months. 4 of 5 young born to 5 immune monkeys which received additional immunization with live measles virus during pregnancy showed a greater degree of immunity and resisted challenge with live virus carried out at various times between the 1st and 22nd months of life. Some evidence was obtained of the passage of measles virus through the placenta to the foetus in experiments on pregnant rabbits, guineapigs, mice and monkeys [the strain of measles virus used in the work is not stated, but it was apparently able to multiply and cause viraemia in small laboratory animals]. *D. J. Bauer*

IMMUNITY

HIRSCH, J. G. **Comparative Bactericidal Activities of Blood Serum and Plasma Serum.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 15–22.

Plasma serum, the liquid exuded after clotting of cell- and platelet-free plasma, is compared with blood serum, that collected after coagulation of whole blood.

Rabbit plasma serum shows practically no bactericidal activity on *Bacillus subtilis, Bacillus megaterium* and a strain of *Staphylococcus aureus,* while rabbit blood serum shows this activity to a high degree. Release into serum during the clotting process of a bactericidin for these Gram-positive organisms depends upon the presence of platelets, not leucocytes; when platelets are present during the coagulation of plasma a heat-stable antibacterial agent is formed or released which has a capacity to kill such Gram-positive organisms equal to that of blood serum. Rabbit blood serum and plasma serum have similar heat-labile lethal effects on enteric bacilli. Human serum, whether from blood or plasma, shows much less bactericidal activity on *Bacillus subtilis* than rabbit-blood serum. Substances formed or released during the coagulation of whole blood, or from the coagulation process itself, appear to be present in blood serum but not in the circulating plasma. *D. A. Cannon*

JANOFF, A. & ZWEIFACH, B. W. **Inactivation of Bacterial Exotoxins and Endotoxin by Iron. *In vitro* Studies.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 23–34. [20 refs.]

Previous work having suggested that in haemorrhagic shock there may be a functional interplay between deranged iron metabolism and bacterial endotoxins, experiments were conducted (with *Clostridium welchii* alpha toxin, *Corynebacterium diphtheriae* toxin and *Escherichia coli* endotoxin) to study the detoxifying power of iron. The lethal effects of aqueous solutions of these toxins after incubation *in vitro* with various agents, were studied in mice, guineapigs and rabbits. Iron counteracted the lethal effects of alpha toxin in mice and of diphtheria toxin in guineapigs; after the incubation of endotoxin with iron, its lethal and tissue-necrotizing effects (but not its pyrogenic properties) in rabbits were counteracted. Other substances tested were copper, magnesium, manganese, zinc, citrate, cysteine, ascorbic acid and versene. Although no evidence is presented to support the view that there is a relationship between the inactivation of endotoxin and the storage iron in the reticuloendothelial system of shocked animals, the observation of an *in vitro* inactivation of endotoxin by inorganic iron warrants consideration of such a mechanism. *D. A. Cannon*

MACKANESS, G. B. **The Phagocytosis and Inactivation of Staphylococci by Macrophages of Normal Rabbits.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 35–53, 7 figs. [12 refs.]

Using the quantitative method of COHN and MORSE [this *Bulletin,* 1960, v. 35, 389], which permits an independent measurement of intracellular and extracellular bacteria during the course of phagocytosis, the author studied the phagocytosis and survival of staphylococci in the presence of rabbit macrophages. *Staphylococcus aureus* was relatively resistant to phagocytosis but in the presence of specific immune serum was ingested at a rate comparable with that of *S. albus* in normal serum: under these conditions more than 90% of bacteria of either strain

were inactivated within 60 minutes. The antibacterial mechanism of macrophages appeared to be fundamentally different from that of polymorphonuclear leucocytes: staphylococci were inactivated more slowly (retaining their morphology for many hours) in macrophages, and disappeared rapidly from the cytoplasm of granulocytes. It appeared that the prolonged survival *in vitro* of some staphylococci was due to variation in the efficiency of the antibacterial mechanism of exudative mononuclear phagocytes: staphylococci which survived early inactivation in macrophages died slowly over many hours, but when recovered from the cells and exposed to fresh macrophages they were ingested and inactivated as readily as bacteria of the original population. *D. A. Cannon*

Miscellaneous

MEDICAL RESEARCH COUNCIL. **Current Medical Research.** A Reprint of the Articles in the Report of the Medical Research Council for the Year 1958–1959. pp. v + 56, 11 figs. on 8 pls. [Numerous refs.] 1960. London: H.M. Stationery Office. [3s. 6d.]

The decision of the Medical Research Council to issue as a reprint these articles on "Some Aspects of Medical Research" from the Report of the Council for 1958–59 [this *Bulletin*, 1960, v. 35, 1071] is most welcome. The 12 subjects have been selected out of the large number of research studies supported by the Council. Every article is clearly written and gives, in as succinct a way as possible, an excellent general picture of the present stage of research. The reference lists have also the virtue, not a universal quality, of including publications by workers unconnected with the Council, in this and other countries.

This small reprint of only 56 pages will be of great interest to many and will also, it is to be hoped, play some part in correcting the opinion which appears to be held by many that Britain is gravely backward in research.

Occupation and Coronary Heart Disease (pp. 1–4).

In a number of surveys it has been observed that coronary heart disease is more frequent in 'light' than in 'heavy' workers and that habitual physical activity or inactivity affects many physiological functions of the body. Whatever their social class, men in 'light' occupations in general show high rates of coronary heart diseases. Factors other than mere physical inactivity may be involved and investigations are proceeding. Puzzling differences within the groups of light occupations exist, for instance the higher incidence of coronary thrombosis in general practitioners than in other doctors; particularly high mortality among radio and telegraph operators; and relatively low mortality among leading Government officials.

Studies on the Chemotherapy of Tuberculosis in East Africa and India (pp. 4–10).

In a report of the World Health Organization it is stated "With the encouraging progress made in the control of malaria, tuberculosis now is the most important specific communicable disease in the world as a whole". This global picture may be illustrated by the estimate that the number of infectious cases in India is between $1\frac{1}{2}$ and $2\frac{1}{2}$ millions. This article tells of the co-operation of the Council's units with national and local agencies in East Africa and India, and with WHO also in India, in the investigation of the particular problems which exist in developing countries. Questions of chemotherapy urgently need answer and among these are mainly those in relation to isoniazid which although it is the "most valuable antituberculosis drug that we possess" has the disadvantage that when given alone isoniazid resistant tubercle bacilli tend to appear in a considerable proportion of cases within a few months.

Clean Air in Operating Theatres (pp. 10–14).

Much work has been done and is being done on reducing still more the risk or airborne infection of a wound during operation. Various aspects of the problem are being explored by certain of the Council's units and by the Public Health Laboratory Service. Some of the investigations deal with methods for preventing or reducing the dissemination of bacteria and with the control of systems of ventilation by positive air pressure.

Human Population Genetics (pp. 15–22).

This interesting article deals with population genetics which is the study of the frequency and distribution of hereditary traits. Continuously graded traits, however genetically determined, are influenced by environmental factors so that it is impossible in principle to separate the effects of nature, and nurture, although their relative importance may be estimated. Among the subject-headings of sections of this article are the genetic effects of radiation, congenital malformations, consanguinity studies and the association of blood group and other genes with disease.

Chromosome Abnormalities and Disease in Man (pp. 22–28).

This article deals first with the suggestions made by the scientists in the past 30 years that some abnormal states of human development might be associated with abnormalities of the chromosomes. There followed 3 important developments in which the Council's staff played a significant part which made possible the remarkable and rapid recent advances in the field of human cytogenetics. These developments were the discovery of sex chromation in somatic cells, the determination of the human chromosome number and new techniques for studying the somatic chromosomes.

New Applications of Electron Microscopy (pp. 28–31).

This is a short description of the possibilities and limitations of electron microscopy with mention of its application to studies such as the structure of muscle, virus structure and the shape of molecules.

The Structure of Viruses (pp. 32–36).

In the summary to this account of the remarkable advances in our knowledge of the molecular structure made in the last few years it is stated: "it may be said that the general features of some of the simpler rod-shaped and spherical viruses have been determined. In both types the mode of assembly of the fully developed infective virus particle from its protein and nucleic acid components into its final geometric form can be readily understood".

The Structure of Muscle in Relation to the Mechanism of Contraction (pp. 36–40).

This is an account of the most recent findings in the examination of muscle by X-ray diffraction and electron microscopy which have led to the new "sliding filament *hypothesis*" of the complex mechanism of muscle contraction.

Interferon: the Prospects for an Anti-viral Agent in Man (pp. 40–43).

In the Council's Annual Report for 1956–57 a description was given of the discovery of interferon at the National Institute for Medical Research. This substance was first isolated from tissue cultures treated with killed influenza virus and has the important property of inhibiting the growth of a number of viruses *in vitro*. Research has advanced in 2 directions—the search for a wide-spectrum anti-viral agent, and fresh investigations by means of the new tool provided by interferon of the processes of virus multiplication. There are short descriptions of the valuable results of these experiments, among which it was found that giving interferon to animals protected them from some virus infections but that the interferon had to be prepared in cells of the homologous animal species. In view of the encouraging results the Council has proposed that large-scale collaborative research should be undertaken and a method of collaboration has been agreed between the Council, the National Research Development Corporation and 3 pharmaceutical firms.

The Arthropod-borne Viruses (pp. 43–48).

The arthropod-borne or arbor viruses, classified as a single group because of the characteristic common to them all that their life span includes a period of growth in an insect, may infect man, causing important diseases or only mild systemic illness or no overt disease at all. There is now a world chain of laboratories for the study of these viruses. The number of viruses which had been isolated was stated in 1959 to be 116. This article gives much information on these viruses and new methods for their identification, their classification and epidemiology.

The Plasma Kinins (pp. 48–51).

The generic name of plasma kinin has been given to the potent vasodilator polypeptide substances which, in the last 10 years, workers in several laboratories have found are formed from plasma proteins under certain conditions. Among their pharmacological properties are a stimulant action on smooth muscle which is slower to produce contraction than that caused by acetyl choline and histamine, and is not affected by the specific antagonists of these substances; the causation of fall of blood pressure by relaxing the peripheral blood vessels and an increase in permeability of the capillaries; and a remarkable capacity for producing pain. There is an account of interesting recent observations which have a bearing on the ultimate elucidation of the physiological role of the kinins. A kinin in a pure state—ox bradykinin—has been isolated at the National Institute for Medical Research and found to be a peptide of 5 amino acids.

Some Factors in the Problem of Inattention (pp. 51–56).

Lack of attention results in remarkably frequent accidents and can also be an important source of economic loss. This article describes the findings of research carried out in a number of centres on this psychological problem. An analogy is drawn between the nervous system and engineering communication systems and the effects of the factors of distraction, fatigue, expectancy and arousal on inattention were examined. These experiments contribute to our general understanding of the problems of inattention. *M. E. Delafield*

PROC. STAFF MEETINGS MAYO CLINIC. 1960, June 22, v. 35, No. 13, 337–89, 9 figs. [Numerous refs.]

Symposium on the Physiologic and Pathologic Aspects of Smoking.

The Effect of Tobacco on Blood Pressure and in Peripheral Vascular Diseases. E. A. HINES, Jr., pp. 337–343.

There is no evidence that the use of tobacco has a regular effect on the level of the blood pressure. In some individuals smoking leads to a sharp rise in pressure and hypertension may occasionally be "cured" if such persons stop smoking. The use of tobacco adversely influences the course of Buerger's disease and probably also affects arteriosclerosis obliterans. Nicotine has a constricting effect on the vessels of the skin of the extremities and this is thought to be the reason for its ill effect.

Effects of Smoking on the Digestive Tract. J. A. BARGEN, pp. 343–345.

In some people smoking acts as a laxative. Presumably it stimulates the bowel and it follows that it should be forbidden in ulcerative colitis and other diarrhoeas. Since smoking stimulates gastric secretion and intestinal mobility it probably interferes with the healing of a peptic ulcer. Occasionally it is responsible for abdominal cramps.

Tobacco Amblyopia. C. W. RUCKER, pp. 345–348.

Tobacco smoke contains substances noxious to the eye. Their presence over many years in a person debilitated by age or malnutrition may lead to an impairment of vision characterized by scotomata spreading between the point of fixation and the physiological blind spot. The condition occurs principally in cigar and pipe smokers; it is very rare in cigarette smokers.

Pathological Effects of Smoking on the Larynx and Oral Cavity. K. D. DEVINE, pp. 349–352.

Smoking is an important factor in the development of cancer of the oral cavity and of the larynx. Cigar and pipe smoking are relatively more important than in the development of lung cancer and are particularly important in relation to oral cancer. Leukoplakia of the mouth and polypoid degeneration of the vocal cords are often associated with excessive smoking and may disappear when smoking is stopped.

Effect of Smoking on Asthma and Emphysema. G. A. PETERS & R. D. MILLER, pp. 353–358.

Clinical and experimental observations show that ciliary action, bronchial secretion and pulmonary ventilation may be altered unfavourably by cigarette smoke. Objective improvement of pulmonary function takes place in some patients with asthma and emphysema when smoking is stopped and patients with asthma, bronchitis or emphysema should not smoke.

Cigarette Smoking a Cause of Carcinoma of the Bronchus? D. T. CARR, pp. 358–367.

The literature relating smoking to carcinoma of the bronchus is reviewed. The evidence satisfies the three criteria which according to YERUSHALMY and PALMER (*J. Chron. Dis.*, 1959, v. 10, 27) are required to implicate a factor as a cause of a chronic disease and it is concluded that cigarette smoking is one of the causes of the principal histological types of bronchial carcinoma.

Smoking and Cancer of the Lung. J. BERKSON, pp. 367–385.

It is unwise to say that smoking is a cause of lung cancer until the carcinogenic mechanism is known. The evidence relating smoking to the disease rests largely on statistics and these may be interpreted in other ways. They may be spurious because of the vagaries of the data or they may have been obtained because non-smokers and smokers differ in other ways relevant to the production of the disease. It is notable that many causes of death other than lung cancer are also related to smoking. The recorded increase in cancer of the lung may result from the survival of susceptible persons who previously would have died of other causes.

Psychologic Aspects of Smoking. M. J. BARRY, pp. 386–389.

Men smoke for two principal reasons: (1) because they have become addicted to nicotine and (2) to obtain oral sensual gratification. *R. Doll*

GRAY, C. H. [D.Sc., M.D., F.R.C.P., A.R.C.S., F.R.I.C.] [Editor-in-Chief.] **Laboratory Handbook of Toxic Agents.** pp. viii + 170, illustrated. London: The Royal Institute of Chemistry, 30, Russell Square, W.C.1. [20s.]

This Handbook is the result of a special committee set up in 1958 by the Royal Institute of Chemistry to consider the problems associated with the use of familiar chemicals and has been augmented by a chapter on the hazards of nuclear radiation emanating from radio-isotopes now in common use in many laboratories. The panel of expert advisers has produced sections on general precautions and prevention, poisonous and corrosive gases, reagents and solvents, precautions against radiations and also a section on first aid in the laboratory.

The chapter on corrosive gases, reagents and solvents (pp. 37–147) covers the widest field of the usual chemical agents used in laboratories, and the specific antidote for each is given together with its MAC where applicable. Modern wide usage of radioactive isotopes requires that personnel handling them should be fully aware of the dangers, and training should be given in the correct handling, care and storage of these materials. Reference is made to the possible emissions from radioactive sources, their penetrating power and permissible doses. The types of laboratory which may use isotopes are graded according to the isotopes being handled and the quantities likely to be involved. The provision of instrumentation for detecting and measuring radioactivity is discussed and the organization necessary to ensure that personnel are not exposed to doses above the maximum permissible level. Decontamination and the disposal of liquid and solid waste is a major problem in user laboratories and the general principles involved are presented.

The section on first aid (pp. 27–34) is compact and covers the majority of emergencies likely to be encountered. It is hoped that when reprinted, this section will amend its references to artificial respiration to include the results of recent experimental work which has suggested that the Holger Nielsen method as shown (and as at present taught by the major first aid societies) may not be effective owing to partial or complete occlusion of the airway due to relaxation of the tongue. It is now recommended that, if the Holger Nielsen method of artificial respiration is used in an emergency, the head should be kept face-downward and not turned to one side, and a folded coat or other material placed under the crossed wrists of the patient, ensuring further extension of the head and a more open airway. Throughout the entire operation great care must be taken to ensure that this extension is maintained.

The committee recommends that in each laboratory a qualified chemist should be appointed Laboratory Safety Officer with the Chief Technician or Steward as his deputy.

The Royal Institute of Chemistry is to be congratulated on the production of a very valuable Handbook which should be available in every laboratory and the notice suggested on the frontispiece indicating the personnel responsible for dealing with emergencies should have a prominent position in all types of laboratory and especially in university, college and school laboratories where the Factories Acts do not always apply.

L. M. Croton

MEDICAL RESEARCH COUNCIL. **Safety Precautions in Laboratories.** 24 pp., 4 figs. 1960. London: 38, Old Queen Street, Westminster, S.W.1.

It has long been recognized that many of the hazards in non-industrial laboratories do not become apparent until an accident has occurred.

This present booklet is an attempt to summarize the

major risks and give guidance to prevention of accidents in handling equipment, materials and tools. For laboratories where specific toxic hazards occur the Royal Institute of Chemistry have produced a handbook, *Laboratory Handbook of Toxic Agents* [see below], but it is felt that the general need for some guidance is achieved in this present publication.

In general, the section on First Aid is up to date especially in the question of treatment of shock and burns. However, recent evidence tends to point to an important deficiency in the only technique of artificial respiration considered. The work of SAFAR *et al.* in America has shown that unless a patent airway is obtained and maintained in the asphyxiated casualty, the Holger Nielsen method may well be ineffective. It is suggested that the head should be kept face-downward and not turned to one side, and a folded coat or other material placed under the crossed wrists of the casualty, ensuring further extension of the head and a more open airway. Throughout the period of resuscitation great care must be taken to ensure that this extension is maintained. This may be difficult for a single-handed rescuer and direct oral resuscitation is now used in many parts of the world as a method of choice in the treatment of asphyxial conditions [this *Bulletin* 1960, v. 35, 339, 340].

L. M. Croton

Book Reviews

SCHILLING, R. S. F. [M.D., M.R.C.P., D.P.H., D.I.H.] [Edited by.] **Modern Trends in Occupational Health.** pp. ix + 313 + [13], 46 figs. 1960. London: Butterworth & Co. (Publishers) Ltd., 4 & 5 Bell Yard, W.C.2. [67s. 6d.]

In 1892 J. T. ARLIDGE'S book *The Hygiene, Diseases and Mortality of Occupations* was published (London, Percival and Co.). Since then there has been a succession of notable books by British authors on what is now embraced in the terms " industrial health " or " occupational health ". *Modern Trends in Occupational Health* is the latest addition. The volume consists of 21 chapters contributed by acknowledged experts in the particular subjects. R. S. F. Schilling, well known for his researches into byssinosis, is the editor. " Modern " signifies the present phase, which, as appears from the several essays, may be regarded as commencing around 1950. Some readers may be interested to find an appropriate comparison in the past; for this the reviewer would suggest *The Health of the Industrial Worker* by COLLIS and GREENWOOD published nearly 40 years ago (London, 1921, J. & A. Churchill).

Owing to limited space a fairly rigid selection of subjects had to be made. Accordingly it was decided to omit general accounts of occupational diseases, occupational skin diseases and working environment, all of which have been the subject of specialized books. This notwithstanding, the absence of a chapter on rehabilitation and resettlement of disabled persons must be regarded as an omission. The book, as stated in the introduction, is written primarily for industrial medical officers, research workers and students of industrial medicine but it is hoped that it may also be of value to others such as factory inspectors, personnel and safety officers, nurses, and the managers and representatives of workers.

To all who have been engaged in this field during the past decade and who have kept abreast of the current literature (which is the purpose of *Occupational Hygiene Abstracts*) most of the contributions will be familiar through previous publications of the same authors. This is no demerit for it is of value to have an author's various papers presented as a whole.

Dr. Schilling contributes the opening chapter entitled The Measurement of Health (pp. 1–19). This is an excellent account of the work of the epidemiologist and a critical evaluation of the methods and tools at his disposal. References throughout his text to the contributions of his co-authors testify to the thoroughness with which he planned the book and edited the scripts. This is further emphasized by the paucity of errors such as: a criteria (p. 15), antedotal (p. 58), chrysolite (p. 63), atalectasis (p. 81), and HILL and FANNING instead of FANING (p. 130). It still seems impossible to agree a standard nomenclature for such terms as " berylliosis " (beryllosis) and " asbestosis (asbestos) bodies ".

Three chapters are devoted to toxicology, with special reference to metal poisonings and pesticides. The exposition of Toxicity Testing by J. M. BARNES (pp. 20–32) merits commendation for its clarity and critical approach. The chapters on industrial pulmonary disease (J. C. GILSON, pp. 50–77) and the measurement of lung function (C. B. MCKERROW and J. C. GILSON, pp. 33–49) reflect the experience and authority of the authors. Incidental to the preceding the question arises: Where do we stand about berylliosis? Is it a metal poisoning and so classified under toxicology or is it a pneumoconiosis? Current views on radiation hazards and occupational cancer are concisely covered. The essays on the mental aspects of health in the individual and the group reflect the importance of these matters in occupational health. Alastair HERON maintains the outstanding quality of his previous contributions on Ageing and Employment (pp. 209–222). As might be anticipated from its authorship (Professor Ross A. MCFARLAND) the chapter on Machine Design and Human Engineering is of high quality (pp. 233–248). This is at once a nice compliment to the author and the pioneer work of the Harvard School. It does, however, beg the question as to whether or not Great Britain has any leader in this field. Noise is a subject of great topical interest and is excellently presented jointly by W. BURNS, Professor of physiology at the Charing Cross Medical School, and T. S. LITTLER of the Wernher Research Unit in Deafness, Medical Research Council (pp. 249–267).

Thus far the emphasis of the essays is on the scientific and research approach. The four final essays are of a

more general nature: The Value of Routine Medical Examinations by L. G. NORMAN (pp. 268–281); Occupational Health Services in Smaller Work Places in Britain by Lord TAYLOR and C. H. WOOD (pp. 282–293); Industrial Law: Trends and Prospects by W. Mansfield COOPER, Vice-Chancellor of Manchester University (pp. 294–305) and The Teaching of Occupational Health by R. E. LANE (pp. 306–313).

All the chapters are fully documented and include an excellent list of references.

Modern Trends in Occupational Health is a worthy addition to the Butterworth Modern Trends Series. Thereby Schilling the editor and his co-authors have enhanced the British contribution to the literature on occupational health. Reference has been made in this review to the spearate chapters but the book must be read as a whole if one seeks to discover the fundamental philosophy which influences the modern trend and foreshadows future development. This book must find a place in the library of every industrial medical officer in Great Britain. He should study it closely and critically. It is also recommended to medical registrars, particularly those who have teaching responsibilities and to all candidates for the M.R.C.P. and D.I.H. Doctors in industry in other countries will find the book valuable as a guide to current work and thought on occupational health in Great Britain. *A. Meiklejohn*

CIFERRI, R. **Manuale di micologia medica.** [Manual of Medical Mycology] Vol. II. Parte Speciale. 2nd Edition. 796 pp., 605 figs. & 15 coloured pls. 1960. Pavia: Casa Editrice Renzo Cortina, Italy. [L. 12,000.]

Volume I of this Manual was reviewed in this *Bulletin*, 1958, v. 33, 1100, and the first edition of Vol. II did appear as promised in 1958 but the entire edition was distributed *hors commerce*. The second edition of Vol. II differs from the first in the addition of a most extensive bibliography (pp. 547–724), sub-divided according to the 16 chapters which it supplements, and in a comprehensive subject index (pp. 725–796) to the whole work.

Vol. II covers the mycoses of man. Each chapter deals with one disease or with a group of related mycoses and each disease is dealt with under a series of standard headings (*e.g.* definition, geographical distribution, aetiology, symptomatology, pathological anatomy, immunology, therapy, etc.), in a manner similar to that popularized by the *Manual of Clinical Mycology* by CONANT *et al.* [this *Bulletin*, 1945, v. 20, 290].

This volume, like the first, shows evidence of having been written by a mycologist rather than by a medical man (for example, pathogens take precedence in the chapter headings, *e.g.* The Mucoraceae and the mucormycoses) and there are further excursions into mycology as instanced by the numerous keys to assist identification of the pathogens. Professor Ciferri did, however, for 30 years work and publish in the closest collaboration with the late Professor P. REDAELLI of Milan, a competent pathologist, and this has enabled him to compile the medical aspects of the diverse mycoses. Many of the clinical illustrations are from other standard texts, some are original, all are of satisfactory quality. While many of the basic facts on the different mycoses appear to be available in a number of English texts there is no current account of the medical aspects of mycoses which is so lavishly documented; this makes the volume of particular value as a book of reference. *G. C. Ainsworth*

BULLOCH, William [M.D., F.R.S.] **The History of Bacteriology. Heath Clark lectures, 1936.** pp. xii + 422, 36 figs. & 16 pls. First edition 1938, reprinted 1960. New York. Toronto. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [30s.]

This book is a reprint of a volume first published in 1938, the text of which was based on the Heath Clark Lectures of 1937, delivered by the late Professor Bulloch; it was the first complete history of bacteriology.

There are 11 chapters in the book, covering 283 pages. Each chapter deals with a major aspect of bacteriological history and the works and conclusions of the early scientists (many too little known) which influenced the course of its development. Thus the first chapter deals with "Ancient Doctrines on the Nature of Contagion" (pp. 3–13) another with "Spontaneous Generation and Heterogenesis" (pp. 67–125) and the ultimate chapter is concerned with the "History of Doctrines of Immunity" (pp. 255–283).

There is a very extensive bibliography which forms an invaluable reference to many original works of immense importance in scientific advancement written by the great figures of medical history.

There is also a section of biographical notes on some of the early workers in bacteriology, which are admirably concise yet rich with biographical references of value to the keen student of history.

The book contains a scholarly balanced account of the development of bacteriology. It is well illustrated with diagrams of apparatus used by Van Leeuwenhoek, Schwann, Pasteur, Tyndall and many others, contains detailed descriptions of many early experiments, and often gives quotations from the conclusions of early workers. It gives prominence to the great deal of little known work on fermentation and spontaneous generation which preceded that of Pasteur while in no way detracting from Pasteur's greatness.

The author has shown the objectivity of the true historian in dealing with his subject. He has described the work of Pasteur and Koch with admirable restraint, refraining from eulogy, has been severely critical only where he found assertiveness unassociated with evidence of experimental endeavour, and has brought prominence to works which merited more recognition than they had hitherto been accorded.

The great fund of information in Professor Bulloch's book has obviously been the result of many years of literary research, yet the book itself can be read rapidly with enjoyment. For the student of medical history it is the only authoritative work on bacteriological history in the English language, yet it is a book which can be read and enjoyed by all members of the medical public. *Frank Russell*

BISSET, K. A. [D.Sc.] & DAVIS, G. H. G. [Ph.D.]. **The Microbial Flora of the Mouth.** 100 pp., 25 figs. (22 on 8 pls.) 1960. London: Heywood & Co. Ltd., Carlton House, Gt. Queen Street, W.C.2. [22s. 6d.]

The authors state in the preface that "The purpose of this book is primarily to provide a straightforward account of the oral flora, from a systematic viewpoint, for the use of dental, medical and bacteriological students and teachers; secondarily, to analyse the available information in the light of our own experience and to organise this information and the appropriate references in a reasonably comprehensible framework for the benefit of those, lacking advanced microbiological experience, who wish to embark on investigations or experimental work in this field, where so much remains to be done." The production of an elementary text which will also interest and be of value to the more advanced worker is no simple task but it has been tackled in this instance with a thoroughness and pleasing directness of approach which have resulted in a large measure of success on both accounts.

The first chapter is concerned with the nature and systematics of the bacterial flora of the mouth. A brief outline of the important characters of the families and genera involved is woven into a suggested evolutionary pattern which provides an interesting basis for much of the later text.

A short chapter dealing with methods of study is intended for the completely inexperienced reader and does no more than outline principles of laboratory technique.

Then follow 12 chapters dealing with the various groups of micro-organisms found in the mouth. Each chapter is short and to the point and includes a summary of the characteristics of the genera and species discussed. Where possible the system of classification and nomenclature of *Bergey's Manual of Determinative Bacteriology* has been adhered to but, as the authors comment, the groups with which they are most concerned are among the least satisfactorily described in that work and departures from *Bergey* are frequent. Where methods of isolation and study are to be found only in original papers, they are described in appendices and the appropriate references are given.

A final chapter is devoted to the part played by the oral flora in disease.

The result is an easily read book with 86 pages of text which will give the student, whatever his bacteriological interests, a sound introduction to the subject while at the same time providing the more advanced reader with food for thought. The bibliography is extensive and well chosen and the book is essential reading for anyone engaged on research in this field.

Experts on the individual groups will certainly find points of disagreement with the authors and the evolutionary concepts which are advanced will not be readily acceptable to all bacteriologists, but it should be remembered that much of this subject is poorly understood and the authors themselves express the hope that such disagreement will stimulate further research. The book contains valuable suggestions for research and emphasizes the paucity of information which exists in many areas. The attention of students should perhaps be directed to the fact that this book is written from the standpoint of the systematic microbiologist and contains much which conflicts with "classical" bacteriological teaching.

The Microbial Flora of the Mouth is well produced, appears to be free from typographical errors and is illustrated by 8 pages of excellent photomicrographs. It can be recommended to bacteriologists, medical workers and dentists alike and should find a place in the reading lists of all departments concerned with the teaching of bacteriology. *John R. Norris*

BROCKINGTON, C. Fraser [M.A., M.D., B.Chir., D.P.H., M.R.C.P., M.Sc.]. **The Health of the Community. Principles of Public Health for Practitioners and Students.** With a Foreword by Lord STOPFORD OF FALLOWFIELD, K.B.E., M.D., Sc.D., LL.D., F.R.C.P., F.R.C.S., F.R.S. 2nd Edition. pp. xvii + 345. 1960. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [35s.]

As expected when the first edition was reviewed [this *Bulletin*, 1954, v. 29, 684] another edition has been called for. It has been subjected to complete revision: it is shorter than the first and is excellent for the readers, medical students and family doctors, for whom it was primarily written.

The general treatment is as before. The outline structure is The History of Public Health; Epidemiological Practice or the Treatment of Disease in the Mass; The Protection of Vulnerable Groups and Epidemiology and Statistics.

The vignettes of public health history are striking and are accompanied by apt quotations from contemporary writings.

The section on co-operation between health visitors and family doctors is just what is needed to make present and future doctors aware of the potentialities. The approach to the vexed question of the place of social workers in public health work is fair and helpful.

There is a forward-looking approach to all the matters discussed and no reluctance to point out the weaknesses of some time-honoured procedures: specially good are those on Health Centres and the world food situation. The Mental Health Act, 1959, is considered fully. The chapters on the "Vulnerable Groups", though admirably compressed, provide a very clear and up-to-date picture of the present position.

Many of the tables give information not usually found in a volume of this size and will be valuable sources of reference for those actually engaged in public health administration. There is a good index and a reasonable bibliography. The book is warmly commended. *Allen Daley*

PRIEST, M. A. **Modern Hygiene for Nurses. Including Bacteriology and the Principles of Asepsis.** pp. vi + 213, 24 figs. 1960. London: William Heinemann Medical Books Ltd., 15–16, Queen Street, Mayfair, W.1. [15s.]

Miss Priest, who is the Principal Sister-Tutor at Bristol Royal Hospital, has written a textbook which covers the requirements of the Personal and Communal Health and the Bacteriology and Principles of Asepsis sections of the Preliminary Examination for the Certificate of General Nursing set by the General Nursing Council for England and Wales. The General Nursing Council publish a detailed syllabus for this examination and the contents of Miss Priest's book follow, item by item, the details of this syllabus. Thus there is an introductory section on the general importance of health to the individual and the community and a general survey of the health services of England and Wales. Section II covers personal health and section III such environmental aspects of hygiene as the control of the safety and purity of food, housing, ventilation, heating, lighting, supply of water, disposal of refuse and sewage and the prevention of infection. The final section deals with bacteriology and the principles of asepsis and antisepsis.

The information given is sound although there are a few minor slips (*e.g.* on p. 4, the date of the main Food and Drugs Act is given as 1958 instead of 1955 and on p. 69, "salmonellae" is mis-spelt). Some parts of the text are repetitive, and in some sections the author has lost track of her subheadings. In the discussion on personal health the word "cleanliness" is overworked, *e.g.* "intestinal cleanliness" and "mental cleanliness." The sections on mental health are meagre and verge on the trite; it would be better if specific reference was made, in the text, to the fact that psychology and human relationships form a different section of the Preliminary Examination and have not, therefore, been covered in this book.

This book adequately accomplishes its modest aim to be a textbook for a specific examination. Its approach and contents, however, raise misgivings about parts of the present syllabus of the Preliminary State Examination.

M. D. Warren

BROUHA, Lucien [M.D., D.Sc.]. **Physiology in Industry. Evaluation of Industrial Stresses by the Physiological Reactions of the Worker.** With a chapter by John A. ZAPP, Jr., Ph.D. pp. xii + 145, numerous figs. 1960. London. New York. Paris. Oxford: Pergamon Press Ltd., Headington Hill Hall. [40s.]

According to Hans SELYE the development of habituation to a stress in the external environment imposes a strain which sets limits to the duration of the acclimatized state. Thus the superlative degree of acclimatization to low ambient oxygen tensions, which has been painstakingly developed during the slow ascent of a Himalayan peak, is accompanied by progressive deterioration in other functions. The final stage of the ascent for this reason must be attempted within a few weeks of reaching the last camp.

There is a wide gulf between this extreme situation and the usual factory occupation where responses to the stresses appear to be mild physiological reactions. All too often, however, owing to heat-producing equipment, or bad design of factories, or the need for protective clothing, a level of heat and work stress develops which calls to arms the defence forces of the body as a whole. Acclimatization is produced but, in spite of incentive payments, productivity remains low and labour turnover high. This book is a record of a successful attempt to evaluate and ameliorate such stresses.

Physical fitness may be defined as that state where work causes minimum upset in the homoeostatic mechanisms and where there is early recovery to the normal pre-work equilibrium. The book relates how the industrial environment may be evaluated in terms of the physiological reactions of the workers. The first section (2 chapters, pp. 3–35) describes the reactions of both sexes, old and young, to physical work. In addition to the traditional measurement of oxygen uptake the effect of work may be assessed by the time required for cardiovascular recovery by recording pulse rate until it returns to pre-work values. There are also some interesting comparisons with values for athletes.

The second section deals with the effects of heat and humidity in 2 chapters (pp. 39–68) and includes a third chapter (the only one not written by the author) on the evaluation of the chemical environment by John A. ZAPP, Jr. (pp. 69–82). It may be common knowledge that cardiovascular stress increases with ambient temperature and reaches a maximum in humid conditions. It is not so well known that the factor limiting maximum performance in the heat is not lactic acid accumulation. There are many other interesting laboratory studies of the effect of heat in limiting work.

The third section discusses job requirements. Jobs in any factory are surveyed and divided into work cycles for further study (pp. 85–108). Two indices used are "cardiac cost" or the total number of beats above normal during work and recovery, and the ratio of total kilogramme-meters of external work to the cardiac cost. These permit classification into jobs producing high, moderate and low reactions. Where the work is too light to produce measurable reactions a strain-gauge-force platform is used. The remaining 2 chapters discuss respectively reduction of stress and fatigue (pp. 109–139) and selection, placement and supervision of workers (pp. 140–165).

A foreword by J. B. WHITE, the Vice-President and General Manager of the Aluminium Company of Canada, describes the remarkable success of the author with both management and men. It is a unique tribute that strikes were averted by his advice regarding conditions of work; both sides knew that this was based on exact measurement.

M. L. Thomson

DAVIS, J. G. [D.Sc., Ph.D., F.R.I.C., M.I.Biol., F.R.S.H.] **Milk Testing. The Laboratory Control of Milk. 2nd Edition.** pp. xiv + 309, numerous figs. 1959. London: Dairy Industries Ltd., 9, Gough Square, Fleet Street, E.C.4. [30s.]

There have been many developments in milk testing since this book was first published in 1951 [this *Bulletin*, 1952, v. 27, 1079] and a new edition was now due. Like its predecessor this volume sets out clearly, and with all necessary details as to equipment, reagents and technique, the standard methods which are now in use in the routine laboratory control of milk. There are many helpful illustrations, and references are provided for tests which

are not carried out as part of routine control but which are required for special purposes. It is essentially a practical book and its strong binding should further commend it to the laboratory worker for whom it is intended. *S. P. W. Chave*

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES established under the joint auspices of UNESCO and WHO. Papers delivered at a Conference [HILL, A. Bradford (F.R.S.), Chairman]. **Controlled Clinical Trials.** pp. vii + 177, illustrated. Oxford: Blackwell Scientific Publications. [20s.]

At a conference in Vienna in 1959 one national group, the British, was charged with the task of presenting each topic to be studied. All the papers were co-ordinated by Professor Bradford Hill, so that overlap was avoided. The book as a whole presents a clear picture of the British concept of the controlled clinical trial—one of the outstanding contributions made to scientific and social medicine during the last 25 years. There are 17 contributors, including clinicians, statisticians and epidemiologists, who together constitute an ideal team for such investigations.

The subjects include: the aims and ethics of controlled trials, construction of comparable groups and other designs of such trials, criteria for diagnosis and assessment, acute infections, pulmonary tuberculosis both at home and in the tropics, rheumatoid arthritis, coronary thrombosis, cancer, and problems of organization, recording, analysis and presentation of results. In brief, it is shown how clinical observations can be organized, collected, and compared with various kinds of controls, so that the results are objective rather than subjective, reproducible, and much more reliable than subjective observations which may be bedevilled by the laws of chance and other factors. This method of randomization, replication, and unbiassed observation in clinical work has been an eye-opener in Britain, and has dispelled many tightly-held illusions. It highlights an experimental approach, though not an easy one, which can be of immense service to medicine, and to the economy generally, in any country which takes the trouble to follow it. Its basic principles can be applied not only to curative medicine, as is done here, but probably much more widely in the social field.

This book, in an earlier mimeographed form, has already aroused widespread interest. It may well become a classic. *H. Stanley Banks*

SWEANY, Henry C. [M.D.] **Histoplasmosis.** pp. xiv–538, numerous figs. 1960. Springfield: Charles C. Thomas, Bannerstone House, 301–327, East Lawrence Avenue, Ill., U.S.A. Oxford: Blackwell Scientific Publications Ltd., 24–25, Broad Street. [£5. 16. 0.]

Histoplasmosis, one of the most important systemic mycoses affecting man and animals, has, since the date of its discovery by DARLING, attracted some of the most eminent research workers in the field of medical mycology. In its acute progressive form it is usually a severe and fatal disease; in its chronic form it presents many clinical and pathological problems, not the least intriguing being its close resemblance to tuberculosis. In fact, the finding of its aetiological agent, *Histoplasma capsulatum*, is considered by many the essential criterion of correct diagnosis.

New facts concerning its diagnosis, epidemiology, geographical distribution and treatment continue to be added to a long list of those already contained in a voluminous literature.

This book, which includes the most important results of past and recent research on histoplasmosis, is the combined effort of 24 leading specialists in the study of this disease, each contributing a chapter on a particular aspect, such as the following: the history of histoplasmosis; the morphology and physiological characteristics of *Histoplasma capsulatum*; saprophytic reservoirs of *Histoplasma*; epidemiology; the serology of histoplasmosis; the pathology of circumscribed localized lesions of histoplasmosis; roentgenographic aspects of histoplasmosis; differential diagnosis.

Clinicians, epidemiologists, radiologists, pathologists, as well as medical mycologists, will find in this stimulating monograph a fascinating account of the results of much patient research work, and of the brilliant discoveries which, from time to time, have served to light the path of progress in the conquest of this insidious and dangerous disease.

The text, which is clearly printed on glossy paper, is well served with many tables and charts of great epidemiological interest, and also with many X-ray photographs and photographs of pathological interest which are well reproduced. *C. J. La Touche*

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